JOURNAL OF NEUROPHYSIOLOGY

[J. NEUROPHYSIOL.]

SEPTEMBER, 1938

VOL. I *Issued Bi-monthly* NO. 5

PUBLISHED BY CHARLES C THOMAS
220 EAST MONROE STREET • SPRINGFIELD, ILLINOIS, U.S.A.

JOURNAL OF NEUROPHYSIOLOGY

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SUBSCRIPTIONS: The subscription rate for the volume of 6 bimonthly issues is $6.00 in the United States, Canada and Latin America, and $6.50 in other countries; it is payable in advance direct to the publisher: Charles C Thomas, 220 East Monroe Street, Springfield, Illinois, U. S. A.

POTENTIAL RECORDS FROM THE OPTIC CORTEX OF THE CAT*

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(Received for publication June 13, 1938)

THE FUNCTIONING of the optic pathway of the cat has been studied by the methods previously employed on the rabbit (Bartley and Bishop, 1933, a & b), namely, by recording the electrical responses of its different elements following single and repetitive shocks applied to the optic nerve. The records of this activity show more specific detail than in the rabbit, presumably a correlate of more specific lamellar differentiation in the cortex of the cat. Magnesium sulphate, 0.25 g/K or less, has proved a suitable anaesthetic, with ether administered during operation. Positions of all electrodes were checked in 20-μ histological sections of the experimental material, and corresponding material is being further studied in Golgi and Golgi-Cox preparations.

Three aspects of cortical relations need to be known for an adequate analysis of the functioning of this cortex as a neural mechanism. Of these, the *anatomical* courses of the connections of the striate area with other parts of the nervous system have been the most extensively studied. The *histological* or synaptic, relationships of the neurons to each other in cell masses such as the geniculate body or the cortex are not so well understood, even to the degree to which neurons themselves have been described. The *time* sequences of the responses of such complicated masses of neurons are no less significant, and it is this temporal aspect of function which is most approachable by present physiological technique. We report here, therefore, on certain time relations of the responses of the various neurons of the optic pathway following specific stimulation of the optic nerve, in the hope that this will assist in the interpretation ot the relationships of cells in the cortex as revealed by histological methods, as well as in the elucidation of the functional machinery by which a visual impulse traverses the nervous system. Finally, in order that the neurons responsible for the observed activity can be identified in the histological picture, the polarity of the response as recorded in different regions is a significant datum.

THE CORTICAL RECORD OF RESPONSE TO A SINGLE STIMULUS

The total response recorded from needle electrodes, one deeper than the other in the cortex, can be differentiated into three concurrent series of events (Fig. 1). The first is a succession of short waves of the dimensions of axon spikes, each of one thousandth second duration, and occurring at intervals of approximately one and a half thousandth second. The first of these spikes

* Conducted under a grant from the Rockefeller Foundation for research in neurophysiology.

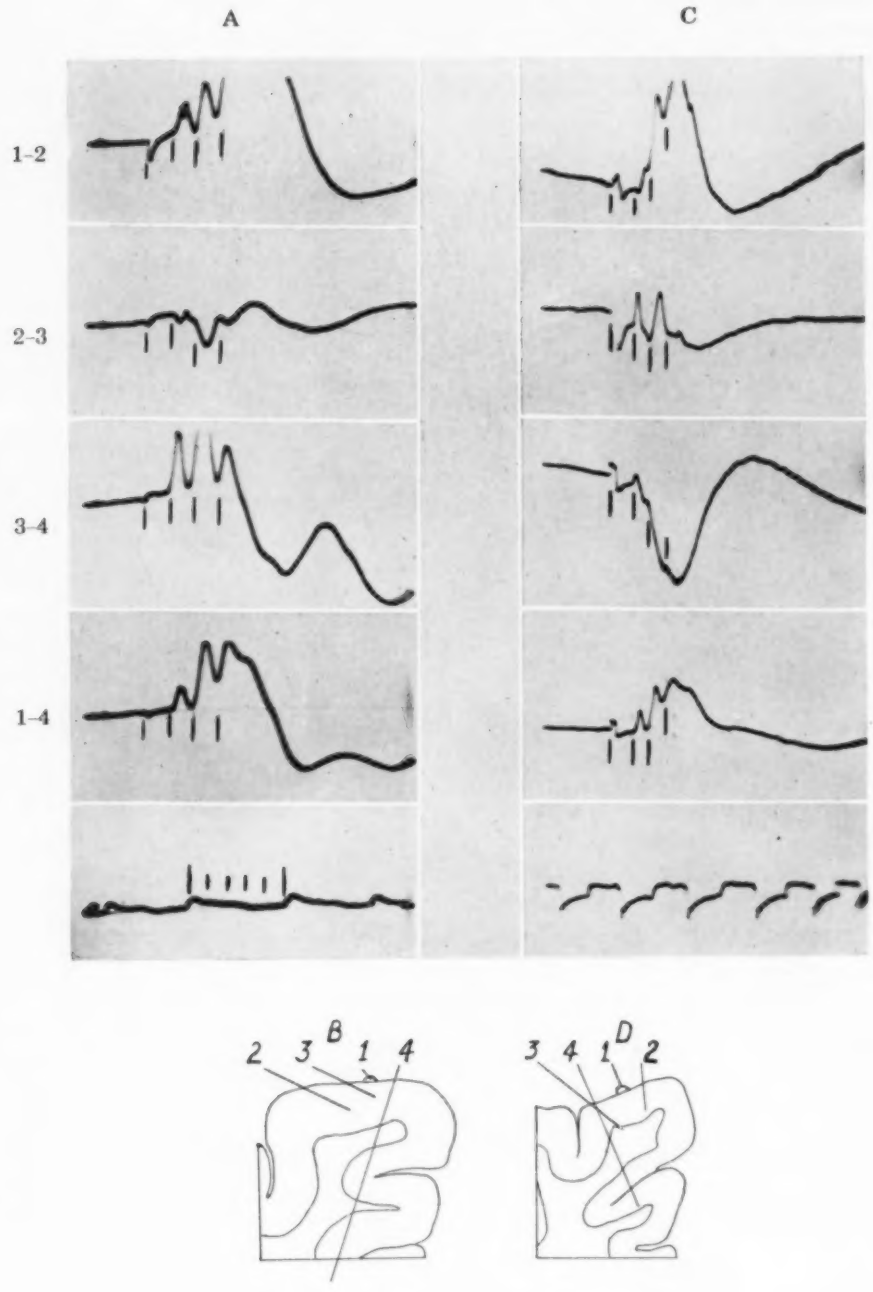

FIG. 1. (*See opposite page for explanation.*)

signalizes the response of the axons of the afferent radiation. The second spike is confined to the cortex, and presumably represents the spread of the impulse through units corresponding to intercalary neurons of the cord. The third can be recorded from well below the cortex, and appears to represent a corticifugal discharge to other regions, the superior colliculus in particular. It is therefore assignable to pyramid or other cells whose axons leave the cortex. In some records, several more such spikes follow the third as a decrementing series, but the first three are always recorded. Whether the later spikes represent repetitive responses of the same elements, or the successive responses of a series, has not been determined.

These spikes were not noticed previously in the responses of the rabbit cortex (Bishop and O'Leary, 1936), but with improvement in technique of recording they can now be seen, though they are much less prominent than in the cat.

The second series of events is recorded as a diphasic or triphasic wave, each phase of 5 to 10 milliseconds duration, which cannot be resolved in our records into elements of the dimensions of axon spikes. This does not necessarily mean that they do not consist of temporal dispersions of such spikes, similar, for instance, to the post-ganglionic responses of the cervical sympathetic after stimulation of its pre-ganglionic nerve (Bishop and Heinbecker, 1932). The first wave of this series usually rises very precisely with the second spike of the former series, that is, it follows the first or afferent radiation wave by the same interval. The later spikes are then written upon this wave as a base line, and the spike series may extend over into the second wave. The two series may be readily differentiated. In certain leads this first

FIG. 1. Responses of the optic cortex of the cat to single optic nerve stimuli. A, electrodes placed as in B, deflection up surface-positive. 1–2, surface of gyrus lateralis to lower margin of superficial pyramids. 2–3, lower margin of superficial pyramids to middle of superficial pyramid layer above it. 3–4, middle superficial pyramids to surface of corpus callosum. 100 mm./mv. reduced ½. 1–4 surface to deep needle at ⅔ amplification of previous records. Note that for record 2–3 the first electrode was accidentally placed deeper than the second, reversing the direction of the deflections, which are thus still surface-positive, with amplitudes in general proportional to distance between electrodes. An exception is that the first spike is higher in the deeper leads. Note also different forms of slower waves at different levels, contributing to the composite record 1–4 from the whole cortex. In the last two records the late downward deflection is the start of the slow negative wave of the alpha series. Lowest record, time from 5 m.s. fork. All records in this and following figures are photographed directly on 60 mm. bromide recording paper with reduction of the oscillographic trace ×½.

C. Similar to A, electrodes as in D. 1–2, surface gyrus lateralis to deep pyramids. 2–3, deep pyramids to bottom of VI layer. 3–4, bottom of VI to VI layer of gyrus fornicatus 1–4, surface to deep needle. First and fourth records, 100 mm./mv. ×½; second and third, twice this. Last record, time from 5 m.s. fork. Note relatively slight development of 1st spike in upper leads, of 3rd spike in middle. The effective reversal of the 2nd and 3rd spikes and slower waves in the lower leads, which were apparently across white matter, may be spurious, representing effective pickup from adjacent cortex dipping into sulci. Further, it is probable that needles thrust into the cortex spring back from their initial position, so that the needle point during recording is above the deepest trace found in the sections. Less than 1 mm. of the tip of each needle is uninsulated, and the needles are thrust in as nearly parallel to the surface as is feasible.

wave is absent, or occurs later, but the spike series is present; and under repetitive stimulation, at the proper degree of anaesthesia, these slower waves following the second of two closely timed shocks may fail to appear, leaving the series of spikes inscribed on a flat base line with the same amplitude as they had previously.

The different phases of this series of slower waves represent responses of different elements, not diphasic responses of the same elements. The first two phases can be differentiated by procedures similar to the one mentioned above, that is, under repetitive stimulation the second element may drop out, and the second wave can normally be recorded below the cortex without the first, when both appear at the cortical level. This sequence of waves in the cat is quite similar to a sequence recorded from the rabbit cortex. The third series consists of still slower waves, which also correspond closely to a series in the rabbit. They have the dimensions of the spontaneous alpha waves, may be repetitive after a single stimulus with the frequency of the cat alpha rhythm, and show the same facilitation for a second stimulus as reported for the rabbit. They undoubtedly represent the response to stimulation of the same alpha mechanism which may also respond "spontaneously" in varying degree without specific stimulation of the optic tract. This mechanism, therefore, has at least a double mode of activation, and other evidence indicates that it is played upon by a variety of pathways.

This system of responses is the nearest to a series of volleys that can be conveniently obtained from the cortex; that is, elements of like properties are responding with the maximum synchronization. Stimulation of the retina by light results in temporal dispersion of like elements, due to repetitive and asynchronous responses of optic nerve fibers to even a weak stimulus (Bartley, 1934; Hartline, 1938). Cortical responses so obtained, therefore, do not show details specific enough to afford more than a rough comparison with the sequelae of single shocks to the optic nerve. We suppose, however, that the same sequence of events occurs following the activation of a given optic nerve fiber by either means, with the obvious possibility that fibers in the nerve of different visual significance may activate different types of responses in the cortex.

Relations of Optic Tract to Cortex

It is found in both rabbit and cat that the cortical responses are maximal following a stimulus less than maximal for all the fibers of the optic nerve. That is, the smaller fibers of the nerve do not contribute to the activation of the cortex. In preparations with lateral geniculate exposed, the lateral and suprasylvian gyri of the cortex remaining intact, the responses recorded from the gyrus lateralis are as near as we can see quite normal. In such preparations the conduction of impulses through the geniculate and superior colliculus has been recorded. The interpretation of these records is complicated by the fact that the active elements are embedded in the electrolytically conducting mass of the brain, and leads from any part of this mass may pick

up stray currents from the optic tract, as leads from the body surface record the electrocardiogram. Analysis of such records will be reported later, but some of the more concrete results are pertinent here.

Records from the optic tract of the cat, as from that of the rabbit (Bishop, 1933), show two main well-separated waves, followed by a decrementing tail of potential. The first wave propagates at about 60 m.p.s., the second at 25, and there is no potential in the C region. The cortical response rises to a maximum as the strength of stimulus is increased sufficiently to elicit a maximal first wave (Figs. 2 and 3), and within the limits of variation of amplitude of the cortical response as activated at different instants, the second nerve potential is followed by no material change in the cortical record, either of amplitude or of configuration. This calls for a correction of a previous indirect inference to the opposite effect (Bishop, 1933, p. 472). Gudden (1886) states that the large fibers of the optic tract terminate in the lateral geniculate, the smaller fibers passing toward the tectum (quoted from Barris, Ingram and Ranson, 1935). Examination of osmicated sections of the tract at the level of bifurcation into superficial and deep rami just distal to the dorsal nucleus shows qualitatively that most of the superficial bundle consists of small fibers, while the deep bundle contains most of the large ones, and the latter fibers in general turn toward the nucleus. More conclusive evidence is that no post-ganglionic second wave can be recorded from leads, one in the white matter just below the cortex, and one on the cortical surface, while the post-ganglionic first wave is well represented there (Fig. 2). Further, the second wave can be recorded from the tract passing to the colliculus without synapsing, together with a low first wave.

From these observations we conclude that the division of the optic tract fibers into two size groups, as indicated by two discrete potential waves, represents a functional division, as has proved true for other nerves; and that allowing for a slight overlap between the smaller fibers of the large-fiber group and the larger fibers of the small-fiber group, such as usually occurs between adjacent groups, the optic cortex is activated only by the group of fibers of lower threshold and larger size. There are probably five times more fibers in the slower conducting group than in the faster. These findings do not compromise Barris, Ingram and Ranson's (1935) observation that individual fibers divide with branches to both the geniculate and tectal tract, but raise a question concerning the function of the "very small fibers," some of which they observed did so. However, they make no specific statement of the actual size of such fibers. The division into the two waves as recorded should fall at a fiber size of perhaps 5μ or less in outside diameter, with a possibility of overlap of the first group to a smaller size.

Temporal Relations and Polarity of Responses

Optic tract and radiation. Conduction in fibers of the optic tract at 60 to 30 m.p.s. requires 0.5 to 1.0 m.s. to the geniculate nucleus. The first wave of the optic tract at this region (Fig. 3) has a duration of not over 1 m.s., of

which approximately 0.5 m.s. is assignable to temporal dispersion through conduction. This leaves about 0.5 m.s. for the duration of the axon responses, which is of the same order as that for peripheral mammalian nerve. This figure is approximate because the necessity of leading from a structure embedded in a conducting medium compromises the precise interpretation of wave form (Bishop, 1937). The interval between the start of this first wave in

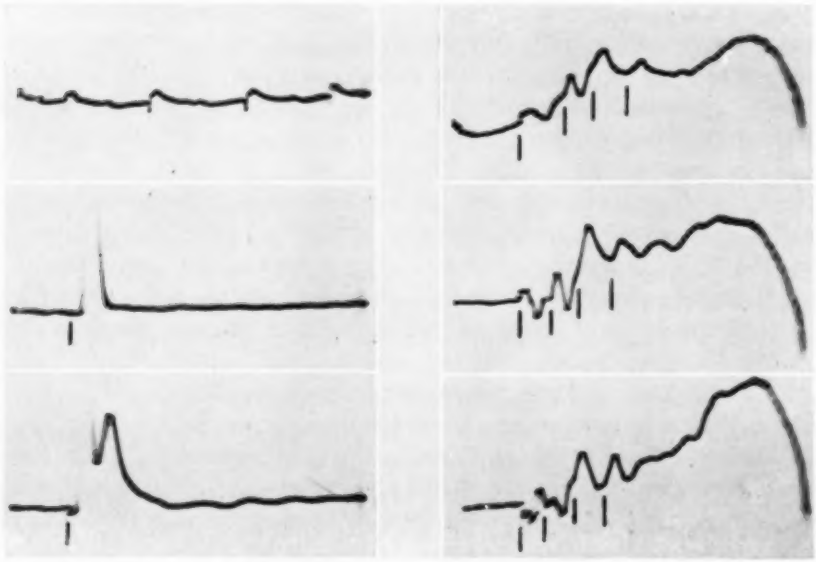

FIG. 2. Relation tract to cortex. Left column, upper, time from 5 m.s. fork; middle, 1st wave maximal led from optic tract; lower, 1st and 2nd waves. Right column, cortical records; electrodes, one on surface of gyrus lateralis, one in white matter of radiation just above ventricle under gyrus suprasylvius. Upper, stimulus strength such that first wave of tract is ½ maximal; middle, 1st wave maximal; lower, 2nd wave maximal. Stimuli are galvanic currents about 0.5 m.s. duration. The first cortical spike due to the afferent radiation is diphasic, the deep lead becoming negative first. Its later occurrence in the upper record results from the start of the impulse only at the end of the galvanic current with a weak stimulus. In the lower record this first spike is distorted by stimulus artefact. There is no significant increase of the cortical record with the increase of stimulus above the maximum for the first wave of the optic tract. For this and the following figure the lateral geniculate and part of the optic tract were exposed by removal of cortex, leaving the gyri lateralis and suprasylvius intact.

the nerve near the geniculate and the start of the post-ganglionic wave in the radiation is 0.6 to 0.7 m.s., with perhaps 0.1 m.s assignable to conduction. The synapse time is therefore of the order of 0.5 m.s., which agrees with that (0.5 to 1.4) reported by Lorente de Nó (1935a) for the oculomotor nucleus. The duration of the post-ganglionic spike recorded from the cortex or from the radiation is again less than 1 m.s., that is, there is remarkably little temporal dispersion through the geniculate synapses. The time of arrival of the afferent radiation impulse at the cortex is from 1.5 to 1.8 m.s. in different preparations, under very light anaesthesia, after the start of a maximal

stimulus. No repetitive responses are observed from the tract or radiation after single stimuli to the nerve at just maximal strength.

Spike series of cortex. From two leads vertically spaced in the cortex, the afferent spike is recorded at any depth except from the most superficial

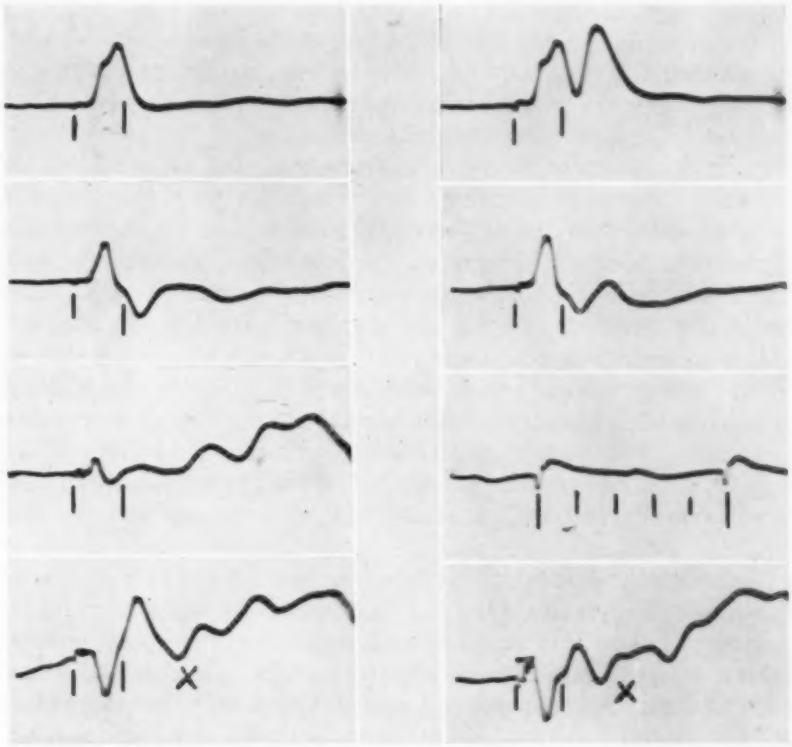

FIG. 3. Relation optic tract to cortex. Left column, 1st wave in optic tract just maximal; right, 2nd wave maximal. Upper, leads from optic tract near geniculate nucleus, and brain stem. The double form of the wave is due to an effective double lead, the edge of the wound exposing the tract distal to the geniculate acting as a virtual lead to give the first hump. 2nd row, L., one electrode into dorsal nucleus of lateral geniculate, the other along optic tract near edge of wound. Up deflection, negativity in tract, downward, negativity in post-ganglionic radiation. R., the 2nd wave of the tract appears just behind the radiation wave. 3rd row, L., leads from surface of cortex to below radiation. A small tract first wave is recorded diphasically, the first cortical spike is the low elevation at the position of the radiation response in the record above, followed by two more spikes and the crest of the slower wave. R., time 5 m.s. 4th row, leads from surface of cortex to geniculate. L., first wave of tract recorded downward, radiation response upward as exaggerated first cortical spike. R., the second wave of the tract fills the gap between first two cortical spikes at x. The top row, 50 mm./mv.; 2nd, 100 mm./mv.; rest, 200 mm./mv.; $\times\frac{1}{2}$.

layers (Figs. 1 and 3), and the deeper of two electrodes is always negative to the more superficial. This is presumably because between any two electrodes so placed, exogenous fibers end at cortical synapses, and thus more fibers pass the lower of two electrodes than the upper. This is not true of the second spike,

which may be either diphasic or virtually monophasic in either direction. The interpretation of this finding is reserved until the histology of these preparations has been studied in more detail, but the fact serves to differentiate this spike from the subsequent ones, which are uniformly surface-positive. This difference might be correlated with the fact that cells of certain types have processes oriented in random directions with respect to the cortical strata, while others such as the pyramids are oriented vertically.

The fact that the third and following spikes are surface-positive, that is, that the lower of two electrodes is rendered negative, at any depth in the cortex, presumably means that more elements are active at the lower levels. This might signify that more of the neurons responsible for these spike discharges lie in the lower strata, but more probably means that a greater number of axons of such cells pass the lower of two electrodes, by the number that originate between them. In this sense the polarity of the record does not indicate the direction of conduction, nor does it measure the magnitude of the response at one electrode region, but is rather an index of the histological organization of the cortical neurons. For instance, a *uniform* distribution of active cells throughout the cortex with axons leaving via the white matter should cause by their simultaneous discharge a *progressively increasing* negativity from surface to deep layers. This same distribution of potential should also result from axons entering via the white matter with endings uniformly distributed upwards, but with conduction in the reverse direction from the above.

The passage of the geniculate synapse occupies 0.5 m.s.; the longer interval between spikes at the cortical level (1.5 m.s. from start to start) might indicate a longer synaptic delay, or it might involve passage of two or more synapses. If the latter, we have no evidence whatever of the responses of the neurons involved, the intervals between the spikes being free from recordable potentials. Interpreted literally, this sequence involves the responses of three-neuron chains, consisting of, first, the afferent neuron with cell body in the geniculate, second, an "internuncial" neuron whose axon does not leave the cortex, and third, a pyramidal neuron whose axon leaves via the white matter. In certain records we have observed a spike recorded from the region of the superior colliculus at the time of the third spike of the cortex (Fig. 4), followed, at the colliculus level, but not in the cortex, by a further series of similar spikes. From this we infer activation of the colliculus via the cortex by this spike sequence. In other records a further sequence of spikes at the cortical level may represent repetitive discharges of cortical neurons, but we have not yet traced such discharges beyond the cortex.

This interpretation leaves no place for "self-reexciting chains" of neurons (Lorente de Nó, 1935b) in this particular cortical sequence. There is, however, a suggestion to be made about the function of the multiple connections of the cell networks observable in histological pictures of the cortex. The series of spikes is remarkable in that the spikes do not become progressively longer in duration as the impulses traverse successive neurons, that is, the parallel

discharges in each bank remain in striking synchronization with each other. This should be the result if more than one fiber-impulse were required to fire the next neuron, that is, if summation were necessary. One impulse would then have to wait for reinforcement by a second, and since no repetitive

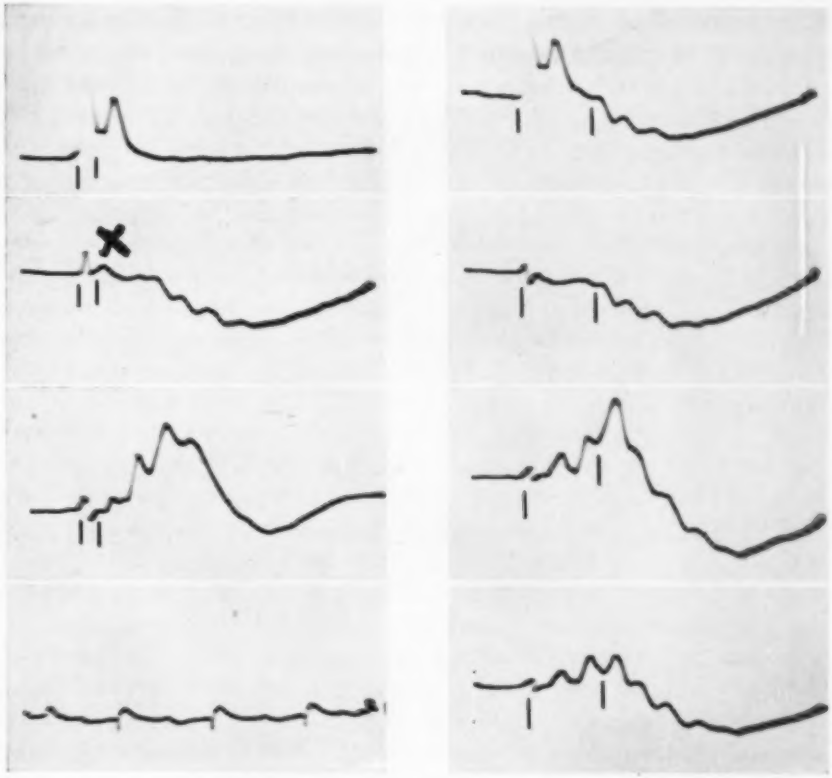

FIG. 4. Relation cortical spikes to colliculus. Upper row, L., two waves recorded from tract and brainstem leads. R., one electrode in tract, one at anterior margin of superior colliculus 1 to 2 mm. below surface. 2nd row, L., electrodes in lateral geniculate and colliculus. The wave marked is a record of the post-ganglionic radiation falling between first and second waves of record above. R., leads from medial geniculate and colliculus. Only stimulus artefact in earlier position than wave of previous record. 3rd row, L., surface of cortex to white matter below. Three spikes and crest of positive wave. R., surface of cortex to colliculus. Three positive spikes from cortex followed by a series of negative spikes from colliculus as recorded in record above. Note that the largest colliculus spike falls at approximately the same time as the last cortical spike, the following spikes being of opposite sign in the record corresponding to the "diphasic" lead. Also, that the second phase of the cortical slower-wave series is represented in the colliculus response. Lower, L., time in 5 m.s. R., same record as directly above it $\times\frac{1}{2}$ amplification. All stimuli maximal for 2nd tract wave.

responses are in evidence, it might have to wait for a response from a parallel neuron which fired somewhat later in the volley. The first neurons active, then, should be unable in general to activate the successive bank of cells until later ones reinforced them, which would thereby prolong the recorded synapse

time and by the same process tend to resynchronize the volley. The multiple connections observed histologically, especially involving certain of the cells with short axis cylinders, might be the means by which such resynchronization was accomplished, as suggested elsewhere from histological considerations (O'Leary and Bishop, 1938).

Perhaps significant in this connection is the effect of increasing depth of anaesthesia, or of rapidly repeated stimulation, upon the cortical responses

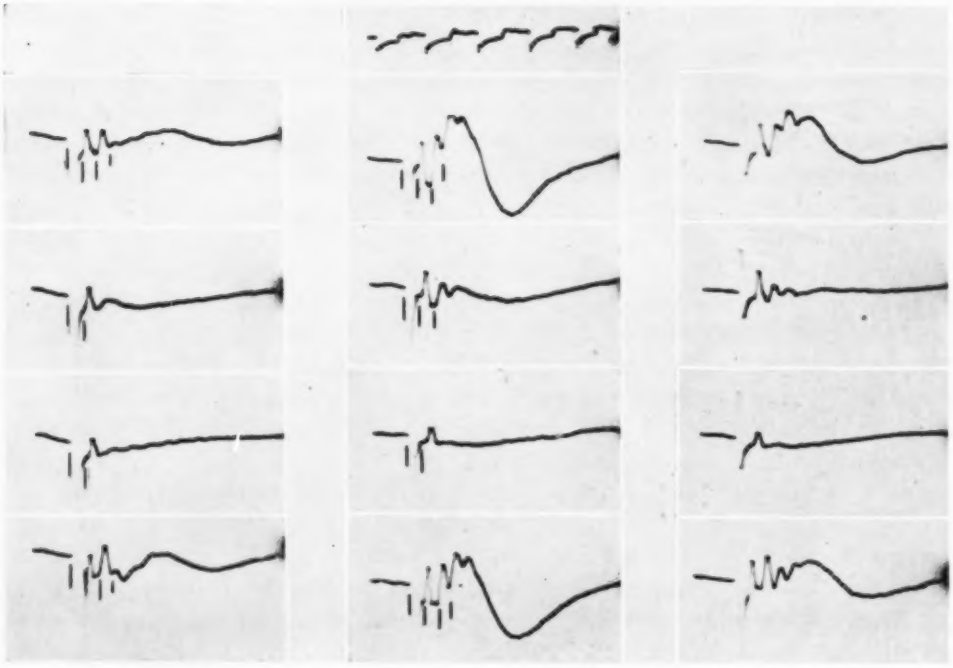

FIG. 5. Effect of ether on cortical record. Left column, leads across middle strata of optic cortex; middle column, across whole cortex, surface to white matter, gyrus lateralis, contralateral to optic nerve stimulated; right column, across whole depth of homolateral cortex. Top row, ether anaesthesia just sufficient to keep animal quiet. 2nd and 3rd rows, increasing ether, respiration still fair, eye wink sluggish. 4th row, recovery. The slow waves disappear before the spikes, the late spikes before the earlier, the afferent radiation (1st spike) only reduced to ½ amplitude when everything else has been depressed. Time at top, 5 m.s. fork. All records 20 mm./mv. on oscillograph, reduced to ½ this in reproduction. The homolateral records are over ½ those of the contralateral cortex in amplitude.

(Fig. 5). The result of either is to decrease the amplitude of later members of the series before the earlier, without materially altering the duration of the spikes. The last spike to disappear is that due to the afferent radiation, which is much more resistant than are the cortical neurons with longer apparent synapse time. Depressive influences in general should tend to increase synapse time and thence increase temporal dispersion in the volley (since different synapses will vary slightly in excitability). This would be expected to reduce the effectiveness of summation at the synapses, and thus tend to block them.

In such a situation given synapses which were essentially alike in excitability, their apparent "refractoriness" or "synaptic delay" might be a function in part of the temporal dispersion of impulses in functionally parallel pathways.

Slower cortical waves. In the foregoing, it appears that if the cell bodies or dendrites of the cortical neurons under consideration give a recordable potential, such potential has the same order of time dimension as does the axon. The problem so far is not to account for the long duration of potentials, but for their brevity. With respect to the second series of potentials, the 5 to 10 m.s. waves, their duration is more nearly what one might expect from post-synaptic axon spikes summed out of phase. The first, surface-positive wave is due to different elements from the second, as shown by various differential procedures; the second is in general half as long again as the first, as might be expected from temporal dispersion across synapses, even if differences in conduction of axons can be ignored in the small distances involved. If, however, the duration of a 5 m.s. wave is to be assigned to dispersion of axon spikes across one bank of parallel synapses, such synapses must have quite different time characteristics from those involved in the spike series. Either they discharge repetitively to a single incoming impulse, or else in apparently coordinate pathways the synapse times may vary over a range of 1 to 5 m.s. Further, the second, surface-negative wave does not start until 5 m.s. or so after the start of the first; in other words, if only one synapse intervenes here also, the time for passage of this synapse must be of that order. This is a longer time than that involved in the slowest synapses of outlying ganglia, those between pre- and post-ganglionic C fibers. With only negative and circumstantial evidence to suggest it, one might look in this sequence of events for neuron chain responses, even for self-reexciting circuits.

Such an explanation, rather than the inference of an essentially slow process in structures other than axons, is suggested by the fact that the second of these waves can be recorded below the cortex in regions occupied only by axons, with time and voltage dimensions of the same order as those found in the cortical wave. As a tentative interpretation, the first wave of this series may be assigned to neurons lying wholly within the cortex, like the second of the series of spikes, and seems to be activated, like the second spike process, immediately by the afferent radiation volley; but it may consist of temporally dispersed and successive, if not repetitive, discharges. The second wave may be assigned to elements whose axons leave the cortex, the temporally dispersed discharges of which are recorded either at the cortical level or below it. The difficulty with this interpretation is that this second wave is generally surface-negative, indicating more active elements passing the upper electrode in the cortex than the lower. Since, however, there are many axons from all levels of the cortex which leave by the plexiform layer, or even which discharge over axon branches both upwards and downwards, the polarity of this second wave is not inconsistent with the histological picture.

A third wave apparently belonging to this sequence, surface-positive, is usually low in amplitude and not always detectable. When the response is

depressed, either by anaesthesia or by repetitive stimulation, the later elements fall out definitely before the earlier, and this whole slow-wave sequence decreases before the spike series is materially depressed. The third wave might signalize the further progress of the visual impulse through the cortex. These waves are recorded differently at different depths of the cortex, the first member of the series being often so low that it raises a question whether no activity is going on at a given region, or whether the activity is equivalent at each electrode; the latter being the obvious inference to be drawn from records at other levels. Further considerations of polarity and amplitude may be postponed pending histological study of the material.

Alpha waves. The sequence of still slower waves, comprising the setting up by a single stimulus of a series of alpha waves, is essentially similar to that of the rabbit, which has been described elsewhere (Bartley, O'Leary, and Bishop, 1937).

Discussion

The foregoing attempt at description, rather than analysis, of cortical activity obviously fails to explain its functioning. The key to the desired explanation is the action of an impulse at a synapse, or rather, the action of complex patterns of impulses at synaptic networks. In view of the current plethora of hypotheses as to how *the* synapse operates, it will not be inappropriate to enquire for a specific situation what this hypothetical action must accomplish. From our records of cortical responses, we infer that there is no single answer; but that certain synapses behave in one way and others in another. The synapses involved in the series of closely synchronized volleys represented by 1 m.s. spikes, for instance, are apparently not operating in the same manner as are those involved in the temporally dispersed waves. Whether such differences are to be referred to differences in temporal or other characteristics of individual synapses, or whether the differences are functions of the patterns of the nerve fiber connections between them, and thus of their interactions, our data do not indicate. From the variety of structure of neurons in the cortex, and the obvious complexity of their synaptic connections, one might infer that individual synapses should differ functionally, as well as that a wide variety of histological patterns should result in a variety of response patterns. At any rate, the problem of synaptic function should be recognized as involving two aspects: first, the question of how any impulse passes any synapse, and second, how an impulse arriving at one synapse on a neuron influences the passage of impulses over other synapses on the same neuron. The multiplicity of synapses on neurons in the cortex indicates the importance of this second aspect for cortical functioning.

The cortical records following a single shock to the optic nerve are perhaps not to be interpreted as records of visual function, although they are obtained from the visual mechanism. Unfortunately, records following the briefest light stimulus to the retina are too diffuse to permit of even such differentiation as single shock records exhibit. At best, the latter indicate merely how the

mechanisms involved can operate under severely simplified experimental conditions. In view of the probability noted above, that the pattern of impulses reaching the synaptic network is a determining factor in the response of such a network, it would be rash to infer correspondences between single shock records and sensory function, and the problem of vision is not the immediate concern of this study. We do not insist that a highly synchronized volley of impulses, from all the axons in the optic nerve, imposes upon the cortex the same pattern of response as does the highly integrated pattern of impulses from the intact retina which is involved in even the simplest turning on and off of a light; to say nothing of the implications of visual pattern and perception of movement. We are rather inclined to fall back upon the shopworn analogy of the nervous system and the telephone exchange, in accordance with which we may study the circuits involved, as circuits. It is, we believe, obvious that much information may be obtained concerning the way these circuits operate, and the nature of the connections involved, by treating the system as a system of *mechanisms*. This may even be an essential preliminary to understanding some of the gossip which the system proves capable of transmitting.

Summary

Responses of the optic cortex of the cat to single stimuli applied to the optic nerve consist of three overlapping series of potential waves differing in their time relations, and separable by simple differential procedures.

The most rapid series consists of three or more spikes, of the order of duration of axon spikes, typically surface-positive. A slower series of two or three waves, the first surface-positive, the second negative, shows a duration of 5 to 10 m.s. for each wave. The still slower series has the dimensions and characteristics of the spontaneous alpha rhythm and presumably involves an activation of the alpha mechanism by the stimulus.

Of the spikes, the first is definitely assignable to the afferent radiation, the second to a cortical neuron whose axons have not been recorded below the cortex. In this sense its neurons correspond to intercalary neurons of the cord. The third spike can be recorded below the cortex, and appears to activate a succession of elements in the superior colliculus.

Comparison of the time relations of responses from the various levels of the optic pathway yields the following information. Of two well-defined waves in the optic tract showing different conduction rates and thresholds, only the faster is associated with a cortical response, the slower propagating past the geniculate to the superior colliculus without a synapse. The synapse time of the impulse at the geniculate level is of the order of 0.5 m.s. The time lost at the synapse between afferent radiation and the second spike neuron in the cortex is 1.2 to 1.5 m.s., and between this latter and the third spike neuron is the same. The slower first wave starts during the second spike.

The configuration of these various components of potential varies with the depth from which they are led in the cortex, suggesting the possibility that they can be correlated with the details of cortical structure.

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A SENSORY CORTICAL REPRESENTATION OF THE VAGUS NERVE

WITH A NOTE ON THE EFFECTS OF LOW BLOOD PRESSURE ON THE CORTICAL ELECTROGRAM

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(Received for publication June 15, 1938)

I. INTRODUCTION

The use of cerebral potentials evoked by various peripheral stimuli has proved of value for the study of cortical localization. Of especial interest are the findings of Bartley and Bishop, Kornmüller, Fischer, Wang, Bremer on the visual area; of Kornmüller and of Bremer on the acoustic area; of Spiegel on the vestibular area; of Bartley, of Bard and his collaborators on the central region; of Ectors on the gustatory and masticatory area; of Walker on the cerebellocortical projection; of Gerard, Marshall and Saul[7] on cutaneous, auditory and optic areas. Kornmüller[10] demonstrated the perfect correspondence of the limits of the visual area, determined oscillographically, with those of the area striata determined histologically.

It seemed desirable to investigate a possible sensory representation of the vagus nerve in the cat's cerebral cortex, for this nerve is composed predominantly of sensory fibers (Foley and Dubois,[6]) including, in the cat, the depressor bundle. It is true that most of these fibers constitute afferent pathways of visceral and respiratory reflexes which do not reach consciousness but this does not exclude the possibility of a cortical representation. On the motor side, a cortical control of visceral functions is now well established (Spiegel,[16] Fulton and Kennard,[8] W. Smith,[14]) and indeed the existence of a reflex viscero-regulator arc passing via the cortex is indicated by the lasting vasomotor disturbances which follow the ablation of certain cortical areas (see Kennard[8]).

Further, the demonstration of a cortical representation for a visceral afferent nerve would furnish a physiological basis for the common view that disturbed coenesthesia contributes to the pathogenesis of various mental affections. Finally, the inhibitory effects, on all the reflex spinal mechanisms, which result from electrical excitation of the depressor nerves (Schweitzer and Wright,[13]) should be reflected in potential changes in the isolated encephalon on stimulating the vago-depressor nerve. These studies led us to examine also the effects of lowered blood pressure on the spontaneous electrical activity of the cerebral cortex.

II. METHOD OF INVESTIGATION

The central end of a cut vagus was stimulated electrically while the spontaneous electrogram of some cortical region was being recorded and any modification noted. All accessible cortical regions were explored. The normal excitation of vagal receptors would have been preferable, but would have been technically difficult and less likely to yield de-

tectable cortical effects. Since depressor nerve fibers are included in the vagus nerve, excitation of this latter is complicated by a fall of arterial blood pressure which it was important to eliminate. This was achieved, and the disadvantages of narcosis obviated as well, by use of the "isolated encephalon" preparation which was introduced by one of us and has already permitted the registration of cortical reactions to varied corticopetal influences with particular clearness.[3] In these experiments, high spinal section practically eliminated all reflex vasodilation, and bilateral section of the vagi similarly eliminated reflex cardio-inhibition.

The cerebral hemisphere was exposed under ether anesthesia, then the vagi isolated in the neck and the trachea cannulated, and finally the suboccipital region exposed and the spinal cord severed from the bulb with a spatula. Artificial respiration was then initiated and the blood pressure registered from the femoral artery. Animals prepared in this way remained in good condition for hours with a blood pressure between 80 and 100 mm. Hg. When it began to fail it could be maintained by a small dose of ephedrine. The vagus nerve was stimulated by induction shocks at 24 to 50 (make and break) per sec. of sufficient strength to evoke a maximal cardiomoderator reflex when the other vagus was not cut. The cortical potentials were led off by a pair of electrodes (Ag—$AgCl_2$—Ringer), about 4 mm. apart, placed directly on the cortex, and recorded by a Mathews or a Dubois oscillograph. The experiments were carried out in a completely shielded room with the inductorium separately shielded. In most experiments the sensitivity was 15 mm. for 100 microvolts. The oscillograph frequencies were 5,200 (Mathews) and 2,000 (Dubois).

III. Experimental Results

With both vagi severed, stimulation of the central end of either one produced no definite alteration of the electrical potentials of the suprasylvian, ectosylvian, cruciate, proreate, occipital or temporal regions or the medial surfaces of the cerebral hemispheres. This negative result cannot be at-

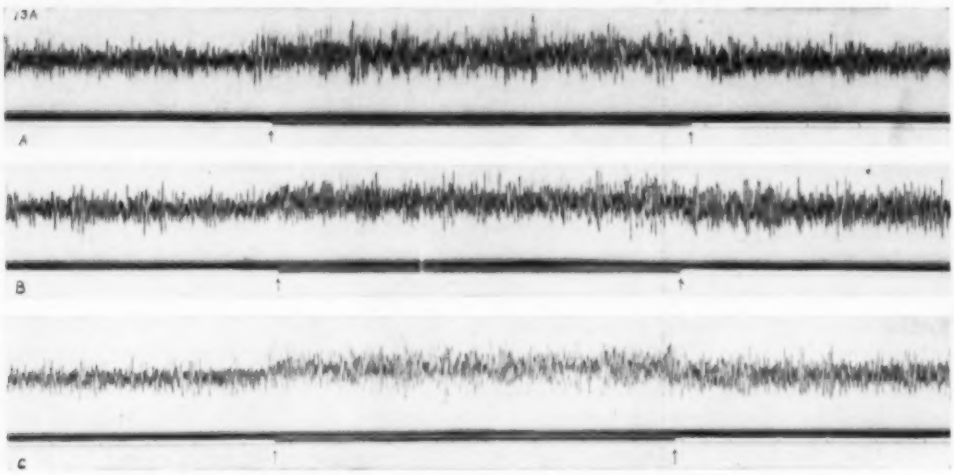

Fig. 1. Cat No. 13. Duration of stimulation indicated by arrows. Time in seconds. Other explanations in text.

tributed to a synaptic block in the bulbar center of the nerve, for it contrasted with the clearcut bulbopontine reflexes of the same stimulation: cardio-inhibition and decreased blood pressure (when the second vagus was not cut), and movements of licking and mastication. Further, after removal of

the eyeball and roof of the orbit, a positive effect was repeatedly obtained on the orbital surface of the frontal lobe (anterior composite gyrus), its potentials being increased both in amplitude and rate. The effect seemed to be slightly more pronounced contralaterally. It was never very marked, but undoubted, since it was obtained with the same technique which repeatedly gave negative results on other areas of the cerebral cortex, even the adjacent cruciate gyrus of the same animal, and since it disappeared when the nerve was ligated proximal to the electrodes. A typical experiment is shown in Fig. 1.

Cat. No. 13. December 1, 1937. Left eyeball removed, and the roof of the left orbit, exposing the orbital surface of the left frontal lobe. Both vagi prepared and sectioned. Spinal cord sectioned at C_1. Artificial respiration. Stimulation with 50 shocks per sec.

A. Blood pressure 90, pulse 120. Stimulation of central end of the left vagus. Leads on orbital surface of left frontal lobe. Definite increase in electrical activity.

B. Blood pressure probably about the same but not recording, pulse 120. Stimulation central end of right vagus. Definite effect on electrical activity of left gyrus orbitalis which outlasted the stimulus about 5 seconds.

C. Stimulation central end of left vagus. Definite effect as in A with perhaps slight after-effect. Blood pressure by puncture of carotid artery 82, pulse 120.

The immediate effect is much the same on stimulating either vagus, but the after-effect is more pronounced contralaterally.

Another experiment in which other areas of the cortex were explored in the same animal is shown in Fig. 2. The differences in the electrograms of the different cortical areas is evident in these records.

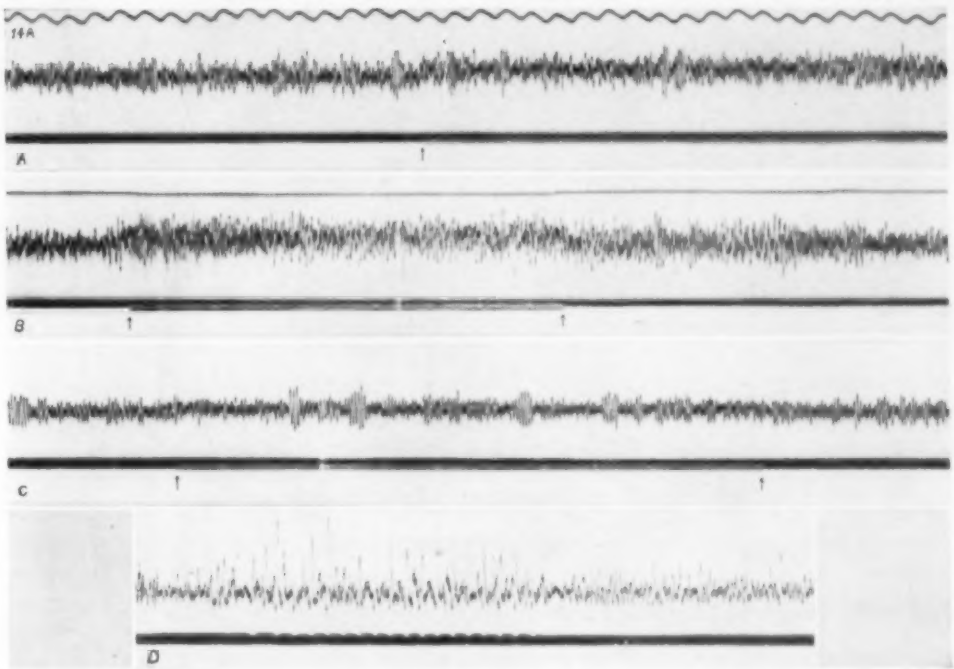

FIG. 2. Cat No. 14. Duration of stimulation indicated by arrows. A and C, cruciate gyrus; B, orbital gyrus; D, ectosylvian gyrus. Time in seconds.

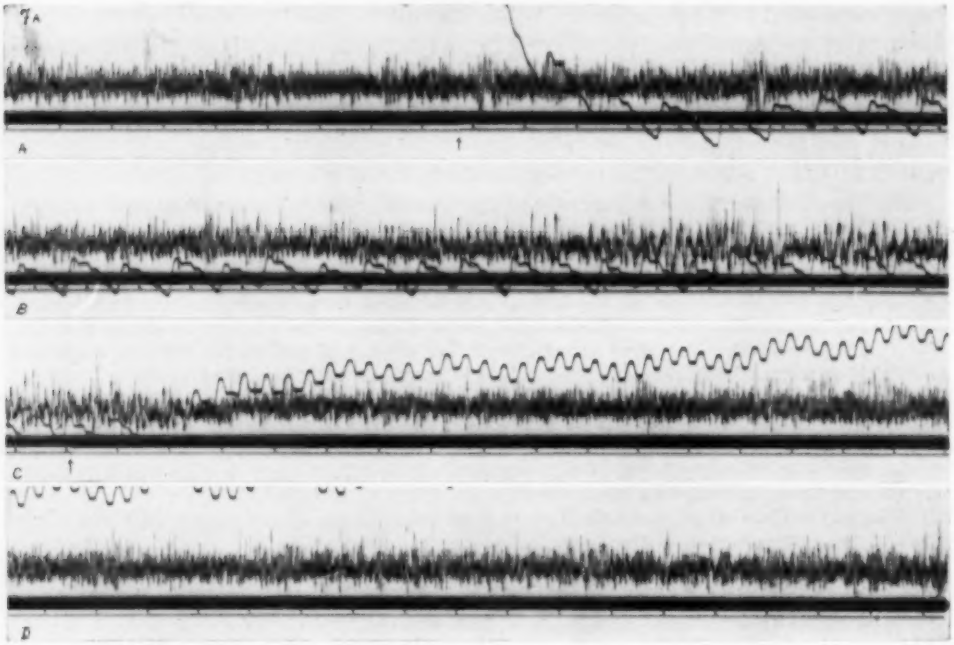

FIG. 3. Cat No. 7. Stimulation indicated by arrows. Time in seconds. Suprasylvian gyrus.

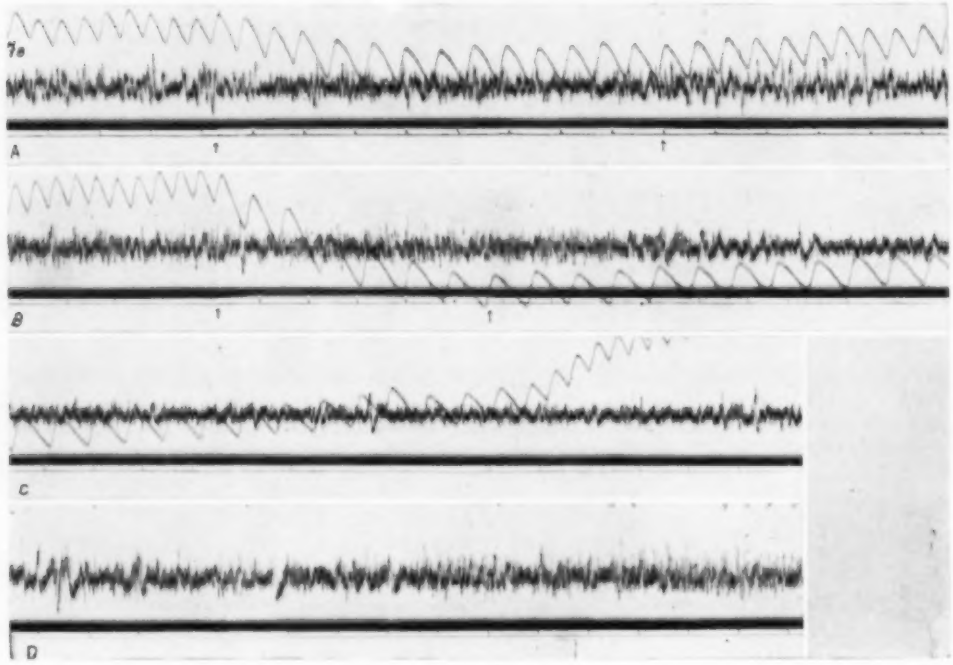

FIG. 4. Cat No. 7. Stimulation indicated by arrows. Time in seconds. Suprasylvian gyrus.

Cat No. 14. December 3, 1937. The left eyeball was removed and the entire frontal pole of the left cerebral hemisphere uncovered. The spinal cord was sectioned at C_1. (Artificial respiration.) Both vagus nerves prepared and sectioned. Stimulation at 50 per sec.

A. Blood pressure 80, pulse 120. Stimulation at central end of the left vagus. Leads on left gyrus cruciatus. No effect on electrical activity.

B. Blood pressure not registering but heartbeat strong at 120 per min. Leads on the orbital surface of the left frontal lobe. Stimulation of the central end of the left vagus. Definite increase in electrical activity which outlasts the stimulus about 5 seconds.

C. Blood pressure not recording but heartbeat strong at 132 per min. Leads on the left cruciate gyrus. Stimulation of the central end of the left vagus. No effect on electrical activity.

D. Leads on left ectosylvian gyrus after exposure of the posterior part of the left hemisphere. Heart weak at 148 per min. The cortex still reacts clearly to stimulation of the left auditory nerve by means of a clacking noise.

Considerable time and some blood were lost between tracings C and D but the cortex was evidently still in condition to react to sensory stimulation.

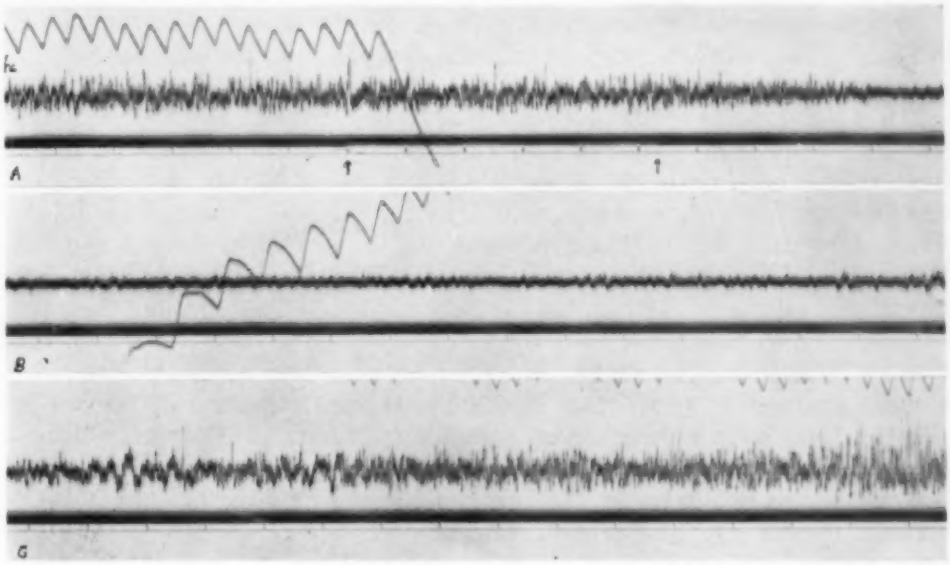

FIG. 5. Cat No. 7. Continuation of Fig. 4.

In all experiments with both vagi severed no effect was ever produced on the state of somnolence of the animal, but in one with the right vagus intact stimulation of the central end of the left repeatedly awakened the cat from a light sleep. This awakening followed a temporary marked decrease in the electrical cortical activity, which was proven to be due to a fall of blood pressure as a depressor reflex through the right vagus. This led us to investigate the effect on the cortical electrogram of variations in blood pressure produced by stimulating the peripheral end of the vagus. A typical experiment is shown in Figs. 3, 4, and 5.

Cat No. 7. November 3, 1937. Both vagi exposed and sectioned. The left cerebral hemisphere exposed and leads on the suprasylvian gyrus. Spinal cord sectioned at C_1. Artificial respiration. Stimulation by inductorium. Time marked in seconds.

FIG. 3. *A.B.C.D.* (Read all records like a book from upper left to lower right.) Blood pressure 100. Pulse rate, 160. Peripheral end of left vagus stimulated with secondary coil at 27 cm. Blood pressure dropped to 60–70; pulse slowed to 66. Form of electrical activity altered. Effect outlasts the stimulus but disappears with rise in blood pressure.

FIG. 4. *A.* Blood pressure 90. Pulse rate 138. Peripheral end of left vagus stimulated. Secondary at 26 cm. Blood pressure dropped to 60; pulse rate to 92. Very little effect on the electrical activity. Pressure afterwards rose to 95 and pulse to 142. The electrical activity became more regular. *B.C.D.* Stimulus was repeated with the coil at 25 cm. Blood pressure dropped from 95 to 40, pulse rate to 72. The electrical activity practically disappeared. The effect outlasted the stimulus about 20 seconds and persisted over 7 seconds after the blood pressure returned to its former level. Blood pressure rose to 100, pulse to 142. Electrical activity much improved and resembles that in Fig. 3.

FIG. 5. *A.B.C.* Blood pressure 80, pulse rate 144. Peripheral end of left vagus stimulated. Coil at 23 cm. Blood pressure dropped to zero and heart stopped. Electrical activity disappeared after about 9 seconds. Electrical activity reappeared 10 seconds after the blood pressure reached its former level. Blood pressure rose to 90, pulse to 186, and electrical activity improved over initial activity before stimulation.

These effects were repeated many times and the records show that a fall of blood pressure below a certain critical level, different for each animal, invariably causes a decrease in the electrical activity of the cortex. With an initial blood pressure of 100, a brief fall of 20 mm. may cause no effect and a longer fall only an alteration in the form of potentials (Fig. 3), whereas in the same animal with an initial pressure of 80, a fall of 20 mm. may result in very marked diminution of electrical activity. The electrical changes follow promptly on the fall of blood pressure but never before several seconds (Fig. 5, B). When pressure is restored, the cortical electrogram returns almost instantaneously (Fig. 3 C) unless the hypotension has lasted more than ten seconds (Fig. 5), and is complete unless the duration of the hypotension was over 20–30 seconds. The return to its previous state is in general preceded by a short phase of augmentation in amplitude and frequency of the waves (Fig. 5 C) related to a phase of high pressure probably due to adrenalin liberation. This phase of increased cortical activity may be accompanied, when the animal was asleep before the vagal excitation, by oculofacial manifestations of awakening. The prolongation of complete cerebral ischaemia for much more than 30 seconds causes irreversible alterations in the cortex even to the complete disappearance of its spontaneous activity and response to sensory stimuli. Moderate hypotension maintained during a sufficient time has a particularly interesting action on the cortical electrogram because at first sight it does not appear to be a depression: the waves, which are reduced in frequency and tend to occur in groups, are greatly augmented in amplitude (Fig. 3 B, and C). This oscillogram is characteristic of sleep and there are other symptoms of this state (closure of the palpebral fissure, downward rolling of the eyeballs, myosis, spreading of the nictitating membrane). Slowing of the heart produces no effect on cortical potentials if the blood pressure is not altered.

IV. DISCUSSION

Little is known of the function or relationships of the orbital cortex of the frontal lobe.[15] Electrical stimulation of this region in man has produced noth-

ing. The area in the cat responding electrically to central vagal stimulation would correspond in man roughly to the area FG of Economo.[5] The areas FF, FG, FH are the most granular in the frontal cortex but their efferent and afferent connections are unknown. We were much surprised to obtain an effect from vagus stimulation in this region; it was tested as a matter of routine exploration. It is on the orbital surface of the frontal lobe, in what we take to be the inferior posterior extremity of the gyrus compositus anterior and, so far as we can judge, is the region from which Smith[14] obtained maximum inhibitory effects on respiration.

The effect of lowered blood pressure on the cortical electrogram is doubtless due to anoxemia, since the alterations it sets up closely resemble those which may be produced by cessation of artificial respiration. Further, the cortical manifestations of sleep are seen in the initial phase of anoxemia (Bremer and Thomas[4]) and during moderate hypotension.

Low blood pressure always depresses cortical electrical activity, though differences in the degree or duration of the fall lead to diverse details, from reduction of frequency and tendency to grouping through simple enfeeblement to complete disappearance. Here again the action resembles that of anoxemia (Bremer and Thomas[4]). We have never observed irritative or epileptiform phenomena, in harmony with the prevalent belief in a subcortical origin of the convulsions observed in sudden hypotensive states in man, notably in the Stokes-Adams syndrome. On the other hand, excitation of the central end of the vago-depressor nerve did not diminish cortical activity except when, due to preservation of the cardiomoderator reflex, it lowered blood pressure. Our experiments, therefore, do not support the hypothesis of a direct inhibitory action by depressor nerves on the cortex or diencephalon.

V. Summary

1. Stimulation of the central end of the vagus nerve increases the electrical potentials of the orbital surface of the frontal lobe of the cerebral cortex. No other portion is affected.

2. The cortical electrogram is very sensitive to alterations in blood pressure, which may vary both its amplitude and form.

3. The effects of low blood pressure are doubtless due to anoxemia since they are practically identical with those produced by cessation of artificial respiration.

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DISTRIBUTION OF DISTURBANCE-PATTERNS IN THE HUMAN ELECTROENCEPHALOGRAM, WITH SPECIAL REFERENCE TO SLEEP

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(Received for publication June 21, 1938)

INTRODUCTION

EARLY study of the cerebral cortex in animals led to the view that this region of the brain acted as a whole. Later work, however, indicated the existence of motor and sensory areas with an extraordinary amount of detailed representation, and also large association areas not directly projected to muscles or sense organs. In man the latter regions make up the greater part of the cerebral cortex. Do the various areas which are known to be functionally different exhibit corresponding differences in brain potential patterns? Particularly, does any change or disturbance in pattern which results from stimulation remain localized or affect the cortex generally?

Recent work in this field has led to somewhat divergent views. Berger (1933, 1934, 1935, 1936) has stressed the activity of the cortex as a whole and Foerster and Altenburger (1935) have also obtained similar records from very different architectonic areas of the human brain during operations. On the other hand Adrian and Mathews (1934) and Adrian and Yamagiwa (1935) originally localized the origin of the alpha rhythm in the occipital lobe, a focus in each hemisphere moving a few cm. right and left or up and down. They attribute the occurrence of a low amplitude alpha rhythm in top and front areas to electrical spread of potentials. Jasper and Andrews (1936, 1938) observed marked differences in pattern of the motor (chiefly beta) as compared with the occipital (chiefly alpha) region. They found little difference between homologous areas of right and left hemisphere in normals; very dissimilar and completely asynchronous patterns in pathological cases. In animals, Kornmüller (1935) has stressed the differences in pattern from cytologically different areas in the rabbit, whereas Rheinberger and Jasper (1937), by permanent electrodes in the cortex of the unanesthetized cat, have been unable to find consistent differences in different areas because of variation in the activity of one region at different times. Stimuli gave rise to specially marked changes in one region but there was also some effect on all other regions.

Our own experiments on man have led us to an intermediate view. There is undoubtedly a localization of certain potential patterns in definite, decidedly large areas of the cortex but there is certainly not the precise localization of pattern that might be expected from the anatomical or physiological map. The brain behaves more or less as a whole so far as electrical activity is concerned. In no respect is this better seen than as the result of disturbances, either internal or due to stimuli sent to the person, awake and asleep. It is

the purpose of this paper to describe the regions of the cortex affected by such stimuli and to present a general picture of potential distribution.

It must be clearly understood that we are not dealing with "evoked" potentials, *i.e.*, potentials appearing in the particular sensory area after peripheral stimulation. In animals these potentials, described by numerous investigators, have a definite form and a relatively short duration. In man their detection through the skull and scalp is unusual. They have been described for light stimuli by Jasper and Cruikshank (1937) in the occipital region, and for touch stimuli by Jasper and Andrews (1937) in the precentral region. Perhaps the flicker potentials of Adrian and Mathews (1934) are to be regarded as evoked potentials.

We are concerned with the more or less continuous spontaneous rhythms whose pattern or appearance may be affected by external stimuli. Three points are of particular interest. Are the waves in different regions of the same general pattern or frequency; are they synchronous and in phase; are interruptions of a train of waves synchronous over large cortical areas? Development of an entirely new recording device with six completely independent amplifier systems has made it possible to study six different regions of the brain simultaneously.

Electrode Positions

Much of the disagreement in interpretation of potential records comes from placements of electrodes. There has been extended discussion of the relative merits of the "unipolar" and the "bipolar" methods, both of which have their own particular advantages. Where two small electrodes are used, the potential difference between regions under each of them is measured. Potential changes in the region between them only show if electrodes are close together and the potential is large. Where one electrode is large ("indifferent") and one small the average of the potential changes under the large electrode compared with the small electrode is measured. A simple method is to have one electrode on a region which remains equipotential so that the pattern will represent only what is happening under the other electrode (the unipolar method). If, however, small electrodes are fairly close together (the bipolar method) they will detect differences of potential within a small area of the brain under them, and consequently give the pattern of potential in that region. However, much higher amplification is necessary. This method has two disadvantages: (1) if the whole area is changing in potential simultaneously, no difference of potential is recorded. (2) If one electrode happens to be in an area of one pattern or frequency and the other in an area of another pattern or frequency both patterns or frequencies will appear.

Therefore, we have adopted the policy of comparing some region on the head with a neutral region, the ear or the mastoid process behind the right or the left ear. Bone is thick over the mastoid process and greatly attenuates potentials, for little brain rhythm is observed when the mastoid is compared with the chin or arm or when right and left mastoids are compared with each other, although the electrocardiogram may appear. Care should be taken

not to use a region just above the mastoids behind the ear for brain potentials may be obtained from this region.

Fundamental to the whole interpretation is a knowledge of the amount of electrical spread (extension of the electrical field) as distinct from the physiological spread of potentials. Detection of electrical spread is dependent on the amplification. Adrian and Mathews (1934) assumed that the electrical spread was considerable and explained the fact that the alpha rhythm between vertex and frontal electrodes is one-third the amplitude of that between vertex and occiput, by electrical spread from the occiput. We believe the explanation is this:—that the alpha rhythm is also present in the frontal region and one-third the amplitude of that in the occiput. There can be very little electrical spread with the amplification we have been using. If so, a potential change of 100μ V in the occipital region should *always* appear at some constant fraction of this value in the frontal region, and *vice versa*. Actually we observe many large potentials from one electrode which do not appear on others.

Gibbs, Lennox and Gibbs (1936) likewise find large petit mal potentials, both spikes (1000μ V) and slow waves appearing from the frontal electrode without a corresponding indication in the motor region, both compared with ear. After one second, however, slow waves synchronous with those of the frontal may also appear in the motor region, but without spikes. In this case there must be physiological (not electrical) spread of a disturbance from frontal to motor regions giving rise to the slow potentials. The evidence is perfectly clear that in epilepsy the spread of potentials over the cortex corresponds with the spread of external clinical signs. When the disturbance reaches the motor region it advances and causes movements which reflect the well known Jacksonian progression.

Only with movements of the eyeball is there evidence of electrical spread of potential. Since the retina is negative to the cornea, quick movements of the eye appear in a record. Simultaneous records from different regions indicate that an excursion corresponding to 150μ V from an electrode just above the eye is reduced about half on the top motor region and one quarter on the occiput. The relative amplitudes differ in different persons. Potentials from eyeball movements, however, are of a totally different character from those of the cortex. They represent rotation of a large dipole, whereas brain potentials represent alternate positivity and negativity of a thin layer in the cortex with respect to the ears or to some other region.

By comparing six different regions of the scalp (front, top and back on both right and left sides of the head) with the mastoid bone, as shown in Fig. 5, we can obtain a very good idea of potential distribution over the whole head. Results may be checked by comparing any of the six electrodes with each other, giving their potential differences directly. Thus, if right and left occipital regions are changing in potential synchronously, in phase and with the same amplitude, no potential will appear between them. If either frequency or amplitude or phase is different, just as marked rhythms may be recorded between right and left occiput as between the occiput and mastoid.

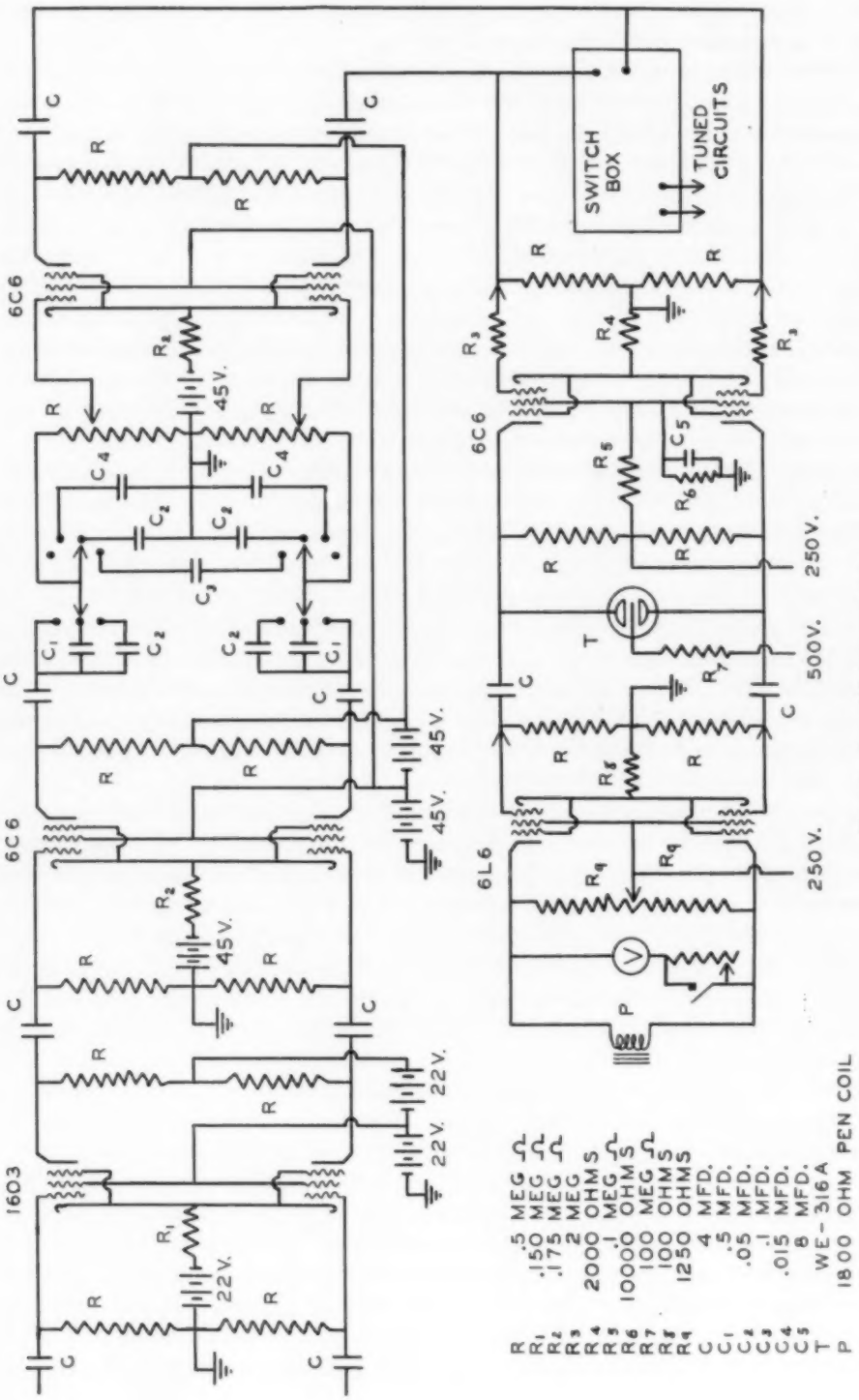


FIG. 1. Amplifying system.

APPARATUS

A convenient and rapid method of placing electrodes is as follows:—attach a ring of rubber (1.5 mm. thick, 5 mm. inside diameter, 10 mm. outside diameter), cut from rubber tubing, to the scalp with rubber cement which dries rapidly and holds firmly. Abrade the skin inside the ring slightly and apply a little Sanborn electrode paste. Push a 5 mm. disk of silver to which a fine wire is attached into the rubber ring against the skin. A drop of collodion over the disk will prevent evaporation. Shielded wires lead from the electrodes to a switching box where twelve connections can be made to six complete amplifier systems in any possible combination, *i.e.*, any grid can be connected to any electrode or any number of grids to any electrode.

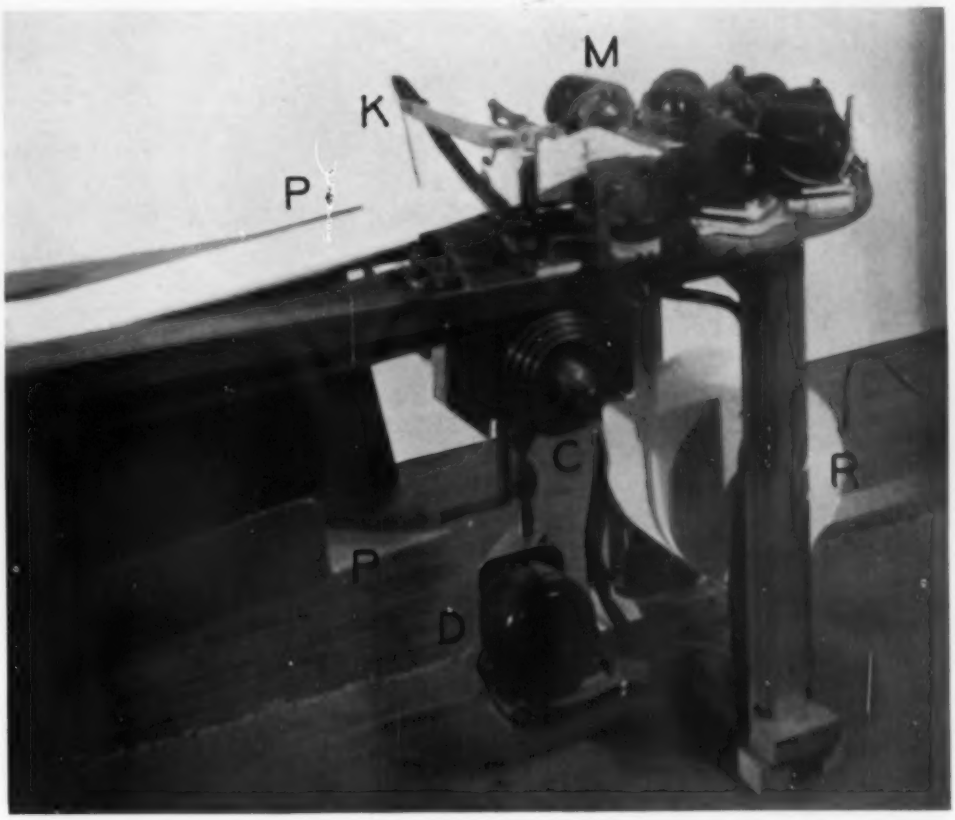


FIG. 2. Paper cutting brain potential recorder showing roll of paper (R) which passes under pens activated by 6 magnets (M) and is cut by a knife (K) each 30 seconds, turned over and laid on a pile (P). The machine is driven by synchronous motor, D. The contact wheels, C, are so arranged that stimuli can be sent to the subject at predetermined times.

The amplifying system is fundamentally similar to that described in 1937, a four-stage push-pull type with special low noise tubes (1603) in the first stage. An additional power stage drives specially constructed dynamic ink writers. So many inquiries have been made regarding the amplifiers that a complete diagram with all details is given in Fig. 1. The new set contains an important improvement which prevents "in phase" potentials, (*i.e.*, those that reach the two grids simultaneously) from being amplified. As a result the subject does not have to be "grounded" at any point and potentials from the heart do not interfere even if one amplifier is attached to leads from an arm while others are attached to

leads from the head. The chief advantage is that the problem of shielding the subject from stray fields is greatly reduced. This result is accomplished by using large cathode resistors connected to negative potentials in the first three stages. Frequency response is practically uniform over the range 0.3 to 46 cycles. Pen deflection is proportional to microvolt input up to a point where neon lamp limitors prevent excessive movement of the pens.

FIG. 3. Enlarged view of electromagnets and 13 pens which write on paper. The flying shears are clearly shown.

The six dynamic pens are arranged in a semi-circle about a moving strip of paper, coming from a roll, seven inches wide. When 30 seconds (1 second = 3 cm.) of recording has occurred the paper is automatically numbered and cut by a moving knife, turned over and placed in position on the previous sheets ready to be bound together for permanent keeping. The recording machine, which has nine different speeds, is shown in Fig. 2 and the electromagnetic ink writers in Fig. 3. Alternating with the six dynamic pens are seven additional pens actuated by small electromagnets. One is a signal pen to record stimuli; the other six record from circuits tuned to any desired frequencies. The appearance of the tuned channels is shown in the records between the brain potential lines. They supplement the untuned record and make it possible to give an accurate figure for the "alpha index" or the index of any other frequency of interest.

DISTRIBUTION OF POTENTIAL PATTERN

Before considering the effect of stimuli, a general picture of the cortical distribution of potential pattern is necessary. We are again impressed with the similarity of records from the same person on different days. Because of

the variation in pattern from person to person it is only possible to make the most general statements; in fact every generalization has its exceptions. Any part of the head connected with any other part will give rhythmic potential differences. The nearer the electrodes, the less the amplitude of potentials and if the two are brought very close together (15 mm.) high amplification is necessary to detect them. As stated previously this means that the two regions must be changing in potential simultaneously and chiefly in phase, as can be proven by comparing each of them with the ears. By such a method of study it is commonly observed that very large regions of the cortex may change in potential simultaneously.

In any one person of the dominant alpha type (see Davis and Davis, 1936) the relative average amplitude of alpha potentials occurring simultaneously in back, top, and front regions may occur in such ratios as 100:60:40 or 60:40:40 or 60:50:0. These figures, given above in μ V, might be continued indefinitely by a careful study of different persons.* Rarely the frontal alphas are larger than the occipital.

If five electrodes are placed on the mid-line in positions 2, 3, 4, 5 and 6, Fig. 4, the recorded amplitudes of simultaneous alpha potentials compared with the left mastoid (7), are shown in Table 1. Note in this particular case, the average values in μ V from front to back are 42, 51, 64, 81, 33. The last value of 33 on electrode 6 is from a point below the inion. The table also shows

Table 1. Amplitude of alpha rhythm.

Electrodes on midline of head front to back in positions illustrated in Fig. 4 are compared simultaneously at times chosen at random over a period of 10 minutes.

Electrode position	Amplitude in microvolts										Average
Front. 7–2	40	50	40	50	40	40	30[1]	40	40	60	43
7–3	50	60	50	50	40	50	40[1]	50	40	70	50
7–4	70	80	60	60	60	70	40	50	80	70	64
7–5	100	100	90	90	100	80	90	100	80	70	90
Back. 7–6	50	30	40	30	20	30	60	40	40[1]	20	36

Electrode position	Amplitude in microvolts										Average
Front. 7–2	20[1]	30	60	40	20	20	50	50	70	60	42
7–3	20[1]	40	70	50	30	40	80	50	70	70	52
7–4	30	50	80	70	40	50	90	60	70	100	64
7–5	120	80	50	100	60	80	70	100	40	30[1]	73
Back. 7–6	50	40	20	40	30	40	20	30	30[1]	10[1]	31

[1] Out of phase.

that the potentials are almost always in phase (occasionally out of phase in front and in far back) and that the distribution varies from time to time, al-

* Since this paper went to press an interesting study has appeared of alpha rhythm distribution by M. A. Rubin (*J. Neurophysiol. 1:* 313–324, 1938.)

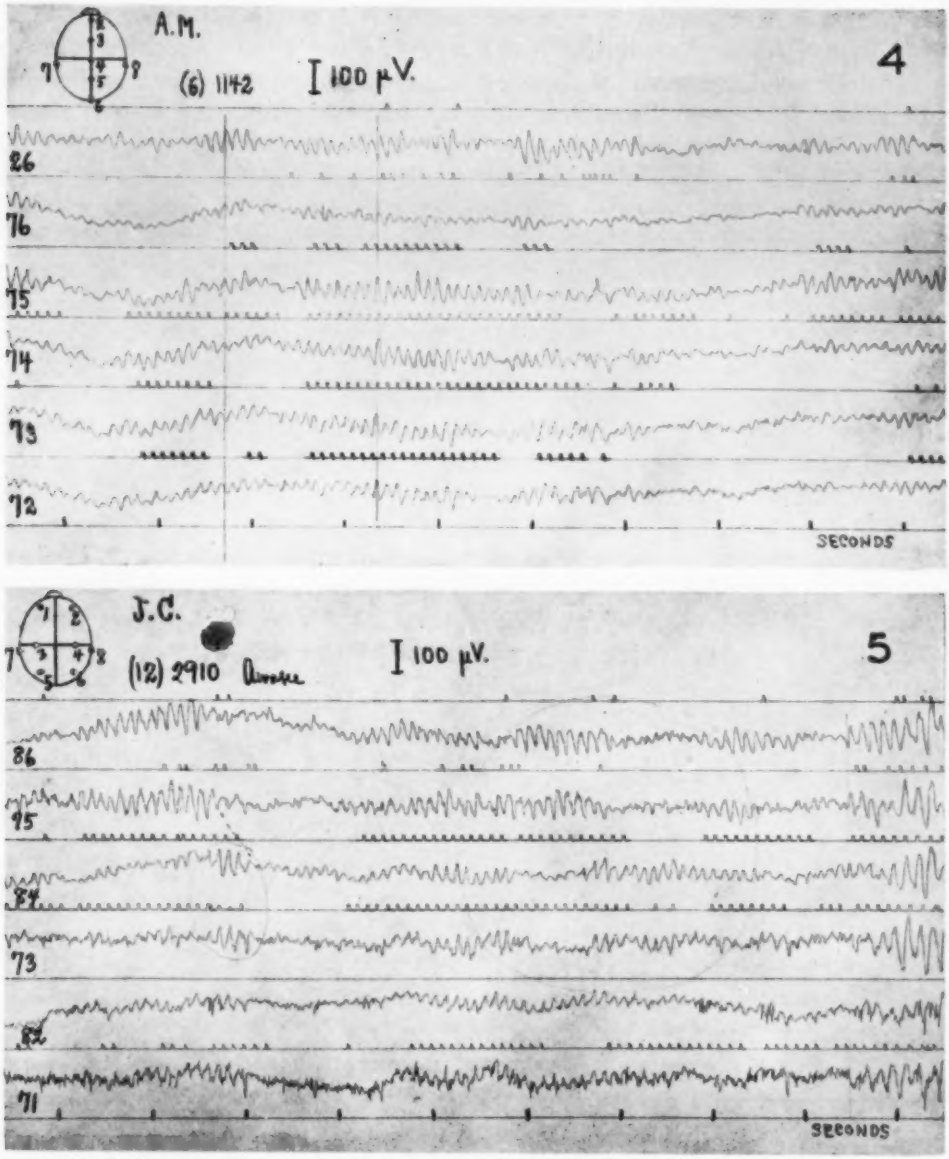


FIG. 4. Alpha type, awake. In all figures the numbers at left indicate placements of electrodes, looking down on head from above as in diagram. Seven and eight are the left and right mastoid bones. When first indicated position is positive the pen moves down. The lines between brain potential records give tuned frequencies. Note that interruptions affect alpha rhythm over whole of head but are more marked in some regions than in others. At the first vertical line 4, 5 and 6 are in phase 2 and 3 out of phase; at the second vertical line all regions of the head are in phase.

FIG. 5. Alpha type, awake. Note that modulation of alpha rhythm usually occurs over whole of head but may appear first on back then on top (in left circle) or may affect back but not top (in right circle). At extreme right note large (130μV) 8 per second waves appearing in all regions. Beta potentials are superposed on the alpha in the front regions.

though the occiput almost always leads in amplitude. This is a frequent picture of alpha distribution, shown in Fig. 4. We have here an excellent example of the dominant alpha type with potential over the whole head changing together, first positive then negative with respect to the ears, ten times a second. The amplitude varies from place to place but the well known interruptions or modulation of the alpha rhythm commonly occur over the head as a whole, only rarely appearing locally in one particular region. Examples of such local distribution are shown within the circles of Fig. 5. In rare cases, large eight-per second potentials may appear simultaneously in all regions, such as those at the right margin of Fig. 5.

In the low alpha type, frequencies are so irregular that a general statement of distribution is difficult. Such a record is shown in Fig. 6. During sleep the alpha rhythm may appear simultaneously in all regions as a result of a tone stimulus. This is shown in Fig. 7, of the same subject. Our observations agree with those of Berger (1933) and with Jasper and Andrews (1936, 1938) that right and left sides show similar patterns; front and back often different ones; also that the beta rhythm, when it appears, is predominantly front and top while the alpha rhythm is predominantly back and top.

Stimuli and Disturbances

By a "disturbance" we refer to any marked change in the regularly occurring potential pattern. These may be spontaneous or they may be the result of external stimuli. No doubt the spontaneous disturbances come from internal stimuli of one kind or another. Thus, when awake, modulation of the alpha rhythm merging into longer interruptions, as already pointed out, *generally* affects, simultaneously, all regions in which alpha rhythm appears. Suppression of the alpha rhythm by light likewise occurs simultaneously in all regions, with occasional exceptions. Jasper and Andrews (1938) have observed light to suppress the occipital alpha but not the frontal alpha rhythm. They also observed the frequency of the two to be different. Occasionally light has little effect on the alpha rhythm, as shown in Fig. 8, where there is only a transitory suppression in all areas.

Davis, Davis, Loomis, Harvey and Hobart (1938) observed in the drowsing state that the alpha rhythm sometimes disappeared on back but not on top during the momentary loss of consciousness experienced at the onset of sleep. However, in looking over a large number of records taken from six different regions of the head simultaneously, one is impressed with the widespread simultaneous changes in widely separated areas, rather than with local differences.

It is in sleep that the most interesting and varied changes in potential pattern occur as a result of stimuli. These were first noted by Loomis, Harvey and Hobart (1935, 1936) and have been observed by Blake and Gerard (1937) in their interesting study of the relation between potential pattern and depth of sleep. Loomis, Harvey and Hobart (1937) have described five successive changes in brain potential pattern representing stages or states of sleep that

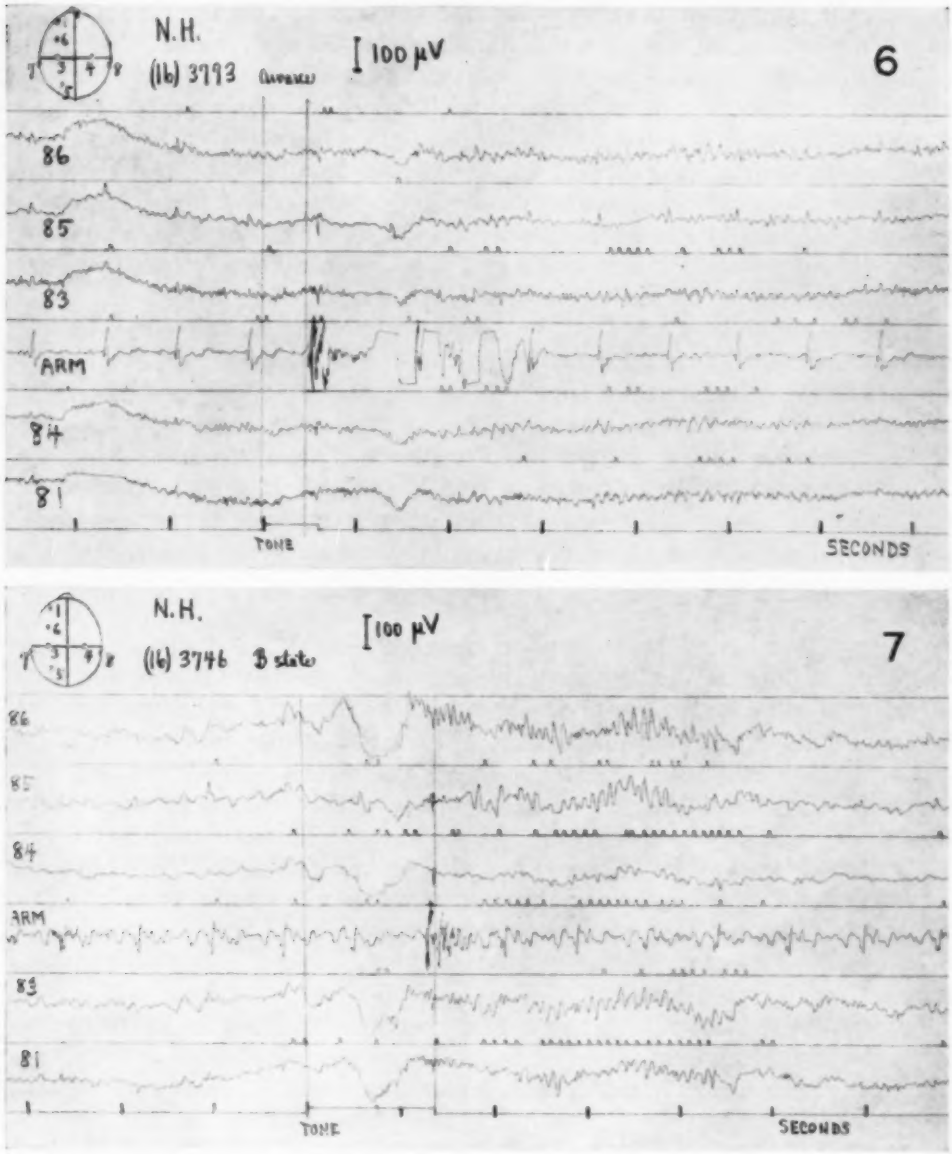
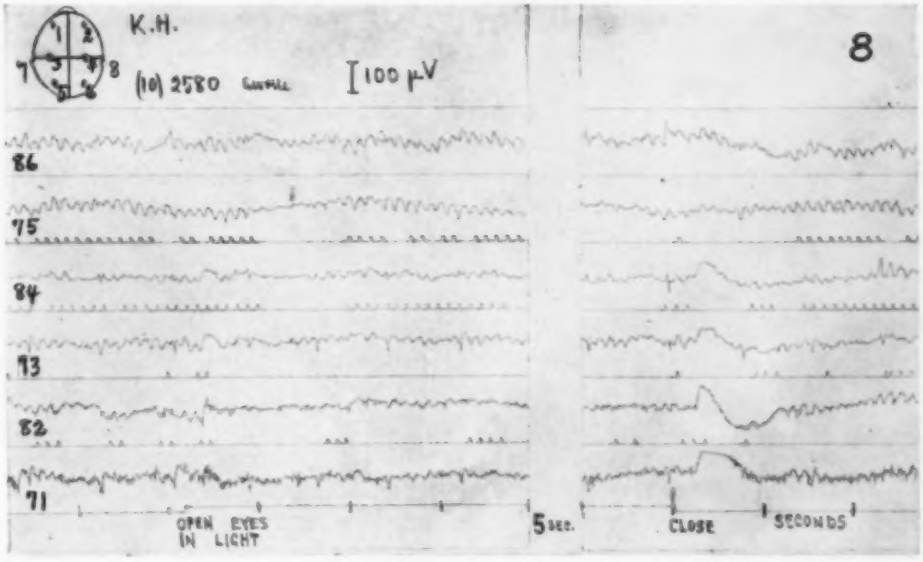


FIG. 6. Low alpha type, awake. Note irregular potentials with beta rhythms on top and front. Electrocardiogram shows on arm electrodes, which also indicate muscle potentials after a tone signal, giving reaction time.

FIG. 7. Same subject as Fig. 6 in B state of sleep; 84 at half amplification. Note long reaction time, indications of a K complex and simultaneous alpha rhythm following a tone stimulus.

are very well defined. These are designated A, B, C, D, and E. During the night a sleeper continually shifts back and forth from one state to another, either spontaneously or as the result of stimuli. The patterns are shown in Fig.



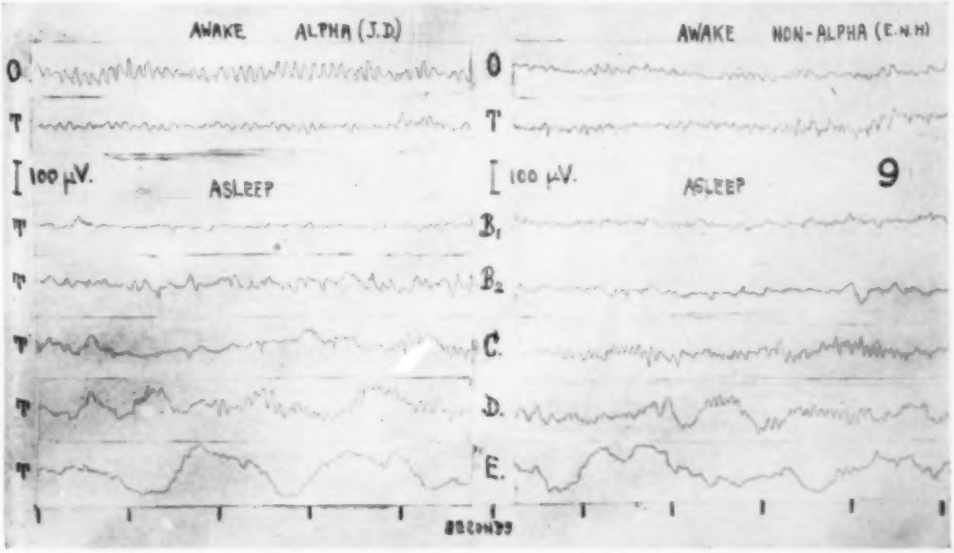


FIG. 8. Alpha type, showing partial suppression of alpha rhythm by light. Note potentials due to eyeball movements when eyes are closed.

FIG. 9. Brain potential activity in an alpha type of person and a low-alpha type, awake and asleep. O = occipital region, T = top of head. B_1, B_2, C, D and E refer to states of sleep. Note that when asleep the patterns are much more alike than when awake.

9. Our present work, based on 25 afternoon naps of 10 persons, has completely confirmed the previous experiments and made it possible to state more definitely the distribution over the head of 14-per-second "spindles," four to five-per-second waves, and the large delta potentials. The E state is rarely

reached in an afternoon nap. A very characteristic response which we call the K wave or complex appears in some states of sleep, either spontaneously or as the result of stimulation.

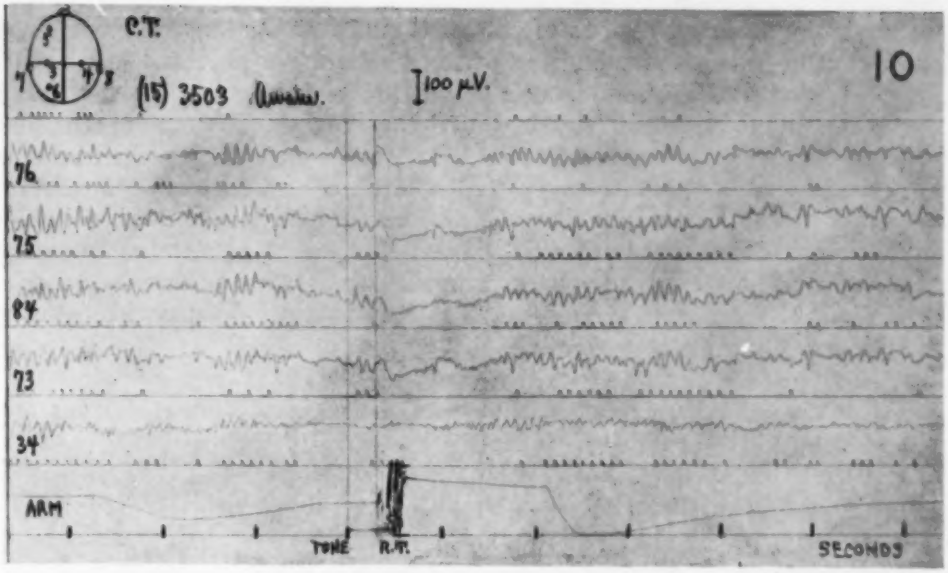
Records of persons which are quite dissimilar when awake, become much alike when asleep. The drowsing state A, with intermittent alpha rhythm, studied in detail by Davis, Davis, Loomis, Harvey and Hobart (1937) reflects the pattern when awake but states B, C, D, and E are fundamentally alike in the alpha and the non-alpha types of individual. This is illustrated in Fig. 9. In the B or low voltage state potential change is of low amplitude over the whole head. When four to five per sec. waves appear, they are largest on the top, then on the front and then on the back. In the C or spindle state the amplitude of spindles is usually largest on the top. They may also be prominent on front or back in some persons. Such a distribution is shown in Fig. 13. In the D state, spindles continue to come from the same regions, while the large random or delta waves of one a second come from all parts of the head. They are largest from the top, less large from the front, and smallest from the back. In the E state, where the spindles become inconspicuous, the delta waves continue from all parts of the head with the same relative distribution in size.

The ability of a subject to respond to a stimulus as he falls asleep was tested as follows. At predetermined times, most often at half minute intervals, stimuli were automatically sent to the sleeper, who was asked to squeeze a bulb in his right hand if he heard a sound (tone from loud speaker) or noticed a light (incandescent lamp, bright enough to be detected through closed eyelids) or felt a weak intermittent induced electric shock applied to his left little finger. Squeezing the bulb made a contact, activating a signal magnet which marked the record. Electrodes on the right forearm also recorded action potentials from muscles involved in squeezing the bulb.

At first, when the subject is still awake, a tone stimulus (not in itself loud or startling) is frequently found to suppress the alpha rhythm if the subject has been asked to react by squeezing the bulb. The phenomenon is illustrated in Fig. 10 where the tone occurs just as a train of alpha waves begins. It will be noted that the alpha rhythm disappears in all regions simultaneously. Many observers have described an effect ("startle effect") when the subject was suddenly "startled," as by a loud unexpected voice, a sudden unexpected touch, etc. There results also a momentary suppression of practically all electrical activity for a short period (one-half to several seconds).

It is likely that the essential cause of a startle effect is a stimulus to which the subject feels he should react with a motor response. Jasper and Cruikshank (1937) have spoken of the "signal value" or "arousal value" of the stimulus. Thus, a faint tone repeated every 30 seconds does not suppress alpha rhythm but if the subject is told to squeeze a bulb whenever he hears the tone, the effect is marked.

With one subject, ten successive trials gave the suppressions illustrated in Table 2. We wish to emphasize that when this effect occurs it is observed over all regions of the head at the same time. Regularly during the B state of sleep and sometimes during the C state, tone, light or electrical stimuli would give



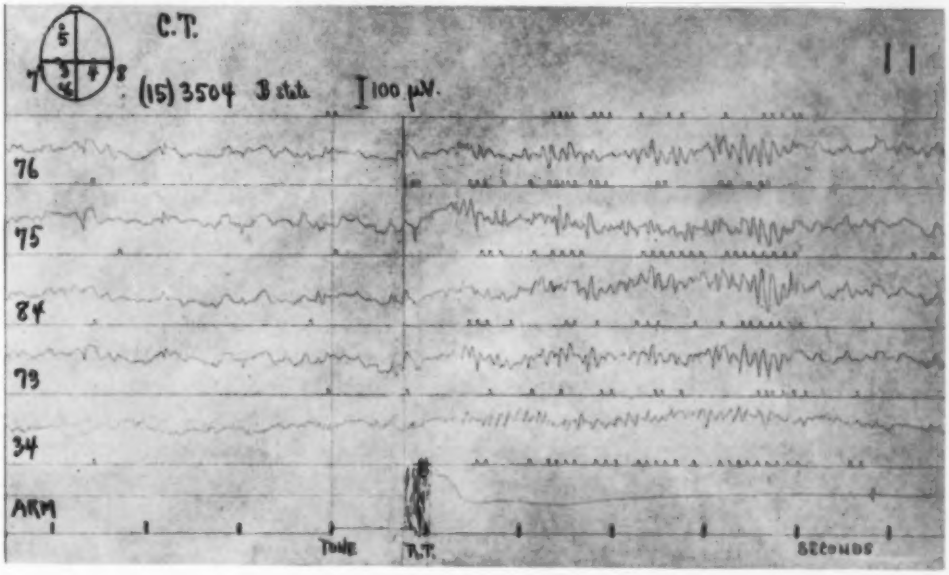


FIG. 10. Alpha type responding to a tone signal by squeezing bulb in right hand which turns off tone, recorded on lower line. Electrodes on right forearm record muscle potential (ARM); 34 records difference in potential of right and left hemisphere over motor region. Note reaction time about 0.3 second. Alpha rhythm which has just started is suppressed simultaneously and begins simultaneously in all regions.

FIG. 11. Same subject as Fig. 10, one min. later, in B state of sleep. Note reaction time 0.75 second and slight delay before alpha rhythm appears on all parts of the head and then disappears simultaneously.

rise to the short bursts of alpha rhythm previously described. Alpha rhythm usually came from all regions of the head which characteristically produce alpha rhythm in the particular person being studied. The rhythm began simultaneously and ended simultaneously in the different regions. A marked effect of this type is shown in Fig. 11. Tone and light were more likely to arouse alpha rhythm than electrical stimulation. If the stimuli were sent in at half minute intervals the subject became accustomed to them and failed to respond by the appearance of alpha rhythm, the adaptation being most marked in the case of electric stimulation of the finger. A change in frequency or intensity (even lowered intensity) of tone or intensity of light or tickle would again start alpha rhythm from large areas of the head simultaneously. Frequently the alpha rhythm began as the stimulus ceased.

Table 2

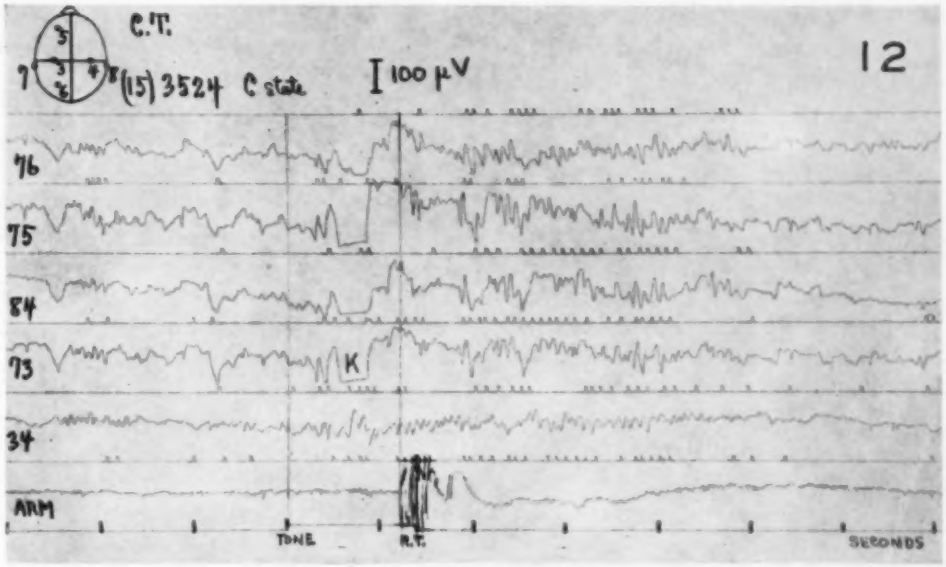
Suppression of alpha rhythm after ten successive tone stimuli, when the subject was asked to respond by moving hand. The figures give time in seconds.

Trial	1	2	3	4	5	6	7	8	9	10	Average
Reaction time	.23	.23	.20	.27	.20	.20	.23	.27	.33	.37	.25
Time of beginning of suppression	.33	.33	.66	1.1	.33	.33	.36	.40	.46	.50	.48
Duration of suppression	.60	.53	1.6	.33	.33	.36	1.6	.36	1.5	.33	.75

This appearance of alpha rhythm over all areas is obviously a shift of the person from one level to another, from the B to the A state of sleep, and not any "evoked" effect of the stimulus, as such. It is the widespread distribution that is notable. The response to light is particularly important and interesting since light abolishes the alpha rhythm when awake and yet gives rise to the rhythm when asleep. The change in reaction time is quite interesting as the subject drops off to sleep. Figs. 10 to 13 show how this gradually lengthens as the character of the brain potentials changes, often becoming over a second in length. We have regularly observed this correlation. Sometimes abortive attempts to squeeze the bulb appear in the record of arm muscle potential without an actual contact being made, as shown in Fig. 13. In the transition between the B and C states of sleep the change in potential pattern occurs over all regions of the head.

When the C state of sleep is reached an interesting and characteristic large potential change occurs as a result of tone stimulation which can be designated a K wave or K complex. This starts in the late B state and appears in the record as a swing down (sometimes up and then down) and then up, corresponding to a negativity (pen moves down) and then a positivity (pen moves up) of the head with respect to ears. It is shown in Figs. 12, 13 and 14. The beginning of a K complex appears in Fig. 7.

The actual potential change may be as high as 200 to 300μ V and the period about a second. The maximum positivity occurs about 0.75 second after the



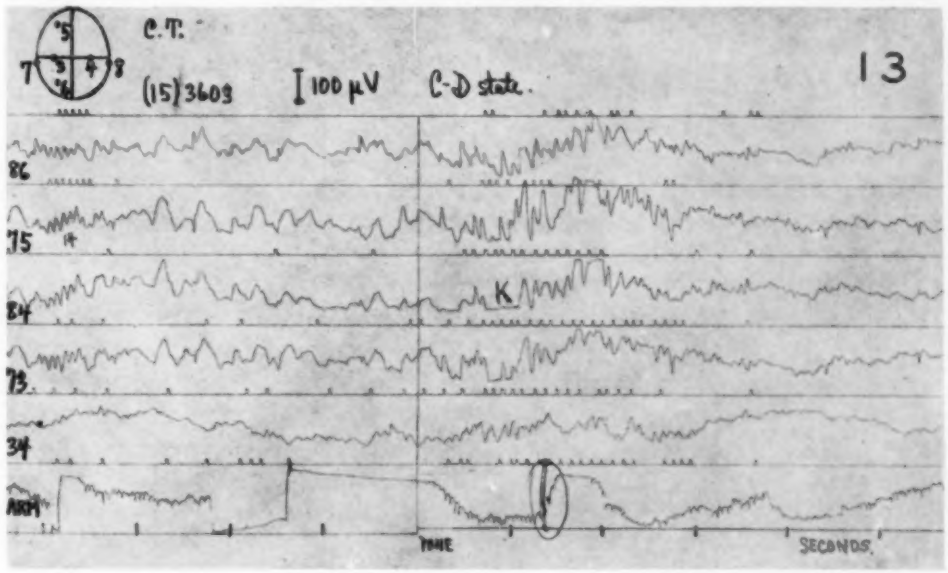


FIG. 12. Same subject as Fig. 10, 10 min. later, in C state of sleep. Note reaction time now 1.25 seconds and the appearance of the K complex, a large slow potential change in which the head becomes negative and then positive to ears, followed by several large potential changes with higher frequency superposed.

FIG. 13. Same subject as Fig. 10, 50 min. later, showing attempts to squeeze bulb not rewarded with success. At left note 14 per sec. rhythm widely distributed over head, followed by 4 per sec. waves and a slight K wave, as a result of the tone stimulus.

tone stimulus begins. With increasing positivity of head there are superposed waves of fourteen to eight per second, rather irregular in frequency. Sometimes there will be several large negative and positive swings in succession resem-

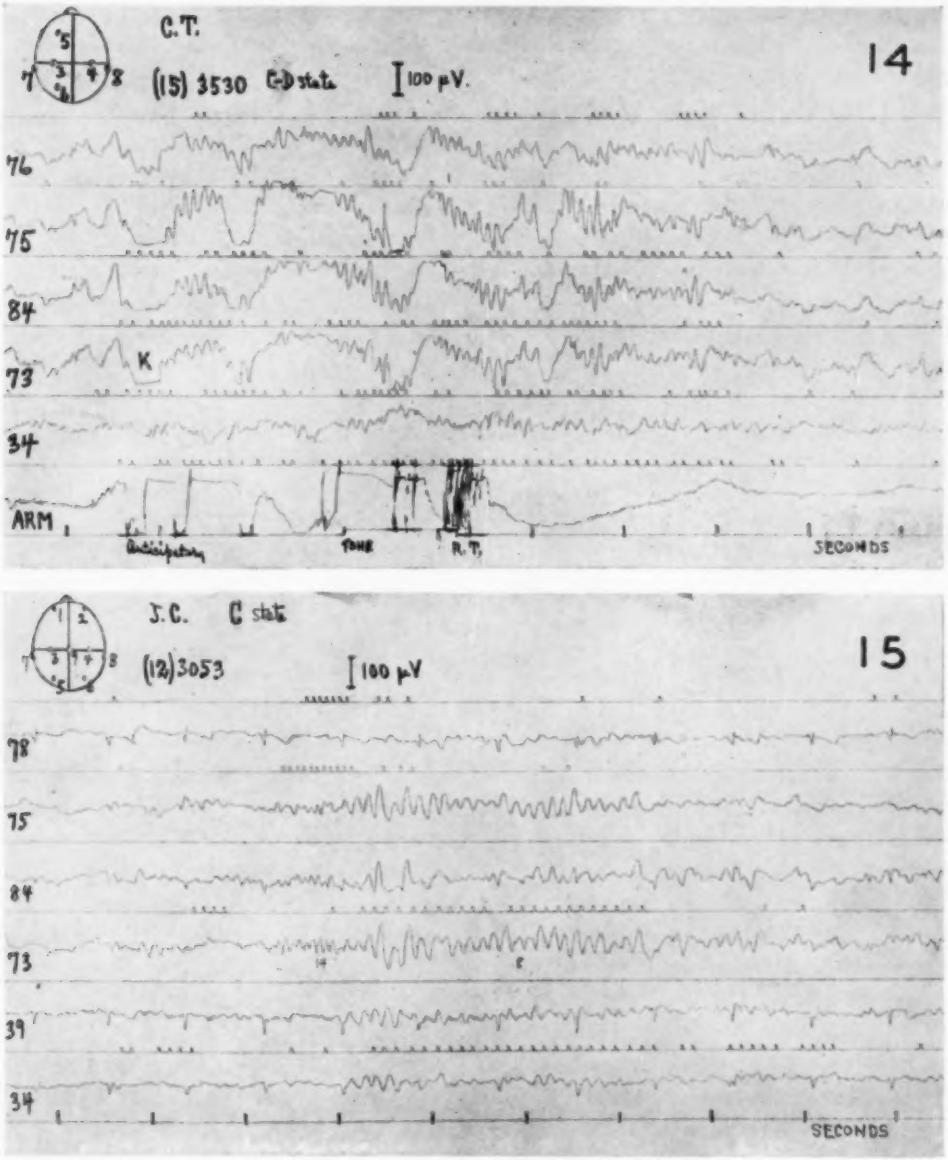


FIG. 14. Same subject as Fig. 10 showing anticipatory attempts to squeeze bulb and final success after 1.1 seconds. Note K complex accompanying anticipatory efforts and simultaneous large potentials on all parts of head.

FIG. 15. Spontaneous change in frequency from 14 to 8 per sec. rhythm during C state of sleep. Note electrocardiogram between mastoids (78) but little brain potential.

bling delta waves. The higher frequency usually appears when the head is going positive to ears. Although the wave regularly follows stimulation, as shown in Fig. 12, it may appear spontaneously in an experiment where the subject

has received no tone stimulus. Sometimes it has been observed to be coincident with a feeble attempt of the sleeping subject to squeeze the bulb, before the stimulus, as shown in Fig. 14. It has appeared in all our regular subjects and is most prominent on top, less on front and least on back of head.

The interpretation of these K waves is difficult and demands further investigation. They are clearly not electrical artifacts nor are they due to movements of the eye balls, as they are larger on the top than on the front of the head. The form is also different. They are not due to movements of head wires as they do not show on electrodes placed over corresponding parts of the right and left hemispheres. Since they have about the same amplitude and period as delta waves, they may perhaps be regarded as the forerunner of these large potentials characteristic of the D and E states of sleep. The K wave is not the only type of disturbance that occurs in the C state. Fig. 15 shows an unusual sudden change from spindles to 8 per sec. rhythm not correlated with any external stimulation. Note that it extends over a considerable area, begins and disappears simultaneously and lasts three seconds. Since the record of this person awake was also unusual we may regard it as decidedly atypical.

The general picture of the cortex that we form from the preceding study of disturbances is of an organ whose parts are so intimately connected that it is unusual to find a disturbance of spontaneous rhythms that is confined to local areas, and almost never confined to a single convolution. When the whole head is "beating" in phase with a frequency of 10 per sec. in different regions, the question arises as to what the relation to individual neurons can possibly be. How can we conceive of a regular pattern which extends from forehead to occiput arising from several layers of cells which are themselves oriented by the complex folding of the cortex? The answer must come from animal experimentation.

Summary

A study has been made of potential pattern from six different regions of the human cortex recorded simultaneously. Combined with the findings of numerous other investigators of human electroencephalography we obtain the following general picture of potential distribution. Right and left halves are fundamentally alike in pattern while front, top and back may be quite different. Beta rhythm is predominantly front and top while alpha rhythm is predominantly back and top. Very large areas exhibit the same pattern or frequency which is often synchronous and in phase, less often out of phase and of slightly different frequency. Amplitude may vary greatly in different regions and at different times. Exceptions have been noted to all the above statements.

In the A (drowsing) state of sleep, patterns reflect those of the person awake but in the B, C, D and E states all persons show fundamentally similar patterns, fourteen per sec. rhythm appearing predominantly on top and large delta waves over the whole of the head.

A disturbance affecting alpha rhythm when awake usually involves simul-

taneously all areas showing alpha rhythm, with delay of appearance in certain regions occasionally observed.

A disturbance during sleep, whether resulting in the return of alpha rhythm, or the appearance of large seven-per-second potentials, or of the newly described large K waves, affects all regions of the head to some extent. The K wave or complex is most marked in the C state of sleep, appearing as a negative and then a positive swing (with respect to ears), with superposed 14 to 8 per sec. rhythm. It regularly results from a tone stimulus but may appear spontaneously, most marked on top, less on front and least on back of disturbance head.

With respect to disturbance potentials appearing on the surface of the skull the cortex thus acts as a whole.

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THE FRIGHT REACTION AFTER SECTION OF THE FACIAL, TRIGEMINAL AND CERVICAL SYMPATHETIC NERVES*

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(Received for publication June 21, 1938)

INTRODUCTION

IN A previous communication[1] observations on reactions of denervated cranial muscles to fright were described. It was noted that two or three seconds after a monkey (*Macaca mulatta*) had been frightened its denervated facial or ocular muscles showed slow contractions. This contraction, termed the "fright reaction," lasted for 30 to 40 seconds. The reaction could be augmented by eserinization and reproduced by parenteral injections of acetylcholin. Injections of adrenalin in small or large quantities failed to produce contractions in the denervated muscles. The contractions produced by fright and acetylcholin were closely parallel in type. They occurred only while the muscles remained denervated. All available data seemed to point to the fact that the fright reaction was due to a humoral agent which in its action on denervated muscles was similar to acetylcholin.

The site of formation and the manner in which the cholinergic substance reaches the denervated muscles are still moot points. It would be possible for the agent to diffuse to the denervated structures from secretion in local tissues or from the blood stream. It is the object of this report to show that the fright reaction is not due to local secretion of acetylcholin. It is well known that electric stimulation of vasodilator nerves causes liberation of acetylcholin at their nerve ending.[2] Such a secretion among denervated muscle fibers would produce in them a slow contraction. Previously in an attempt to eliminate this factor of local diffusion as a possible explanation for the fright reaction the superior cervical ganglion, sympathetic trunk and infraorbital nerves were cut.[1] These procedures did not abolish or materially reduce the contraction associated with fright. Hinsey,[3] however, suggested that the inferior cervical ganglion and uncut portions of the trigeminal nerve might be involved in the local production of acetylcholin within the facial or ocular muscles. There are also other nerves in the regions denervated which may act as a source of local secretion of the parasympathetic substance. To insure complete interruption of the local nerve supply to the face and eye the oculomotor and trigeminal nerves were cut intracranially, while the facial, chorda tympani and part of the pharyngeal plexus, were cut extracranially. In addition the superior middle and inferior cervical ganglia were removed and the carotid artery was denuded.

* This work was aided by a grant from the Fluid Research Funds, Yale University School of Medicine.

Results

Section of facial nerve

In most instances the facial nerve was cut at the exit of the stylomastoid foramen. The fright reaction in the denervated facial muscles appeared 7 to 10 days after nerve section, irrespective of what part or to what extent the nerve was excised. Intracranial or intracanalicular resection, avulsion of the geniculate ganglion, or excision of all branches of the facial nerve yielded identical results. In every instance a typical peripheral facial paralysis with loss of electrical reactions appeared. In some monkeys the skin temperature of the denervated face and ear became warmer, but later grew cooler than the normal side. So long as the muscles remained denervated the fright reaction could be elicited. The sensitivity to acetylcholin reached its maximum about 25 days after the nerve section. Thereafter, with regeneration of the nerve, it diminished unless the heightened sensitivity was maintained by periodic resection of the nerve fibers.

Section of the oculomotor and trigeminal nerves

The technique for section of the oculomotor and trigeminal nerves was the same. Only observations on trigeminal nerve section will be described here as the results of oculomotor nerve section have been reported already.[4] Through a large bone flap the greater, especially the posterior, part of the cerebral hemisphere was uncovered. Such an exposure made it possible to examine cranial nerves III, IV and V. By gently elevating the temporal lobe from its middle fossa, the petrous pyramid and its apex were visualized. Around the cerebral peduncle the trochlear and more anteriorly the oculomotor nerve could be seen. Near its apical insertion the tentorium cerebelli was incised, bringing the trigeminal nerve into view. Two roots were clearly discernible, the smaller being more lateral. Stimulation of these roots caused closing of the jaw, and, with strong enough current, the ipsilateral facial muscles contracted. The latter contractions were abolished immediately after the peripheral facial nerve supply was interrupted. Apparently the abnormal facial contraction obtained on stimulating the trigeminal nerve roots with unipolar and bipolar electrodes was due to electrical spread. Stimulation of the trigeminus nerve more anteriorly in its preganglionic divisions yielded the same responses. Stimulation of the first division caused a dilatation of the pupil and slow retraction of the upper eyelid. The latter responses were similar to those obtained on stimulating the cervical sympathetic, except that there was no piloerection.

The entire trigeminal nerve was cut. In one monkey the incision extended anteriorly to include the Gasserian ganglion. This lesion, in addition to the signs described below, was followed by a herpetic eruption of the skin about the eye. The signs of trigeminal nerve section were: (i) loss of the direct corneal reflex and of sensation over the face; (ii) decrease in pupillary diameter, pseudoptosis and (iii) deviation of the jaw to the ipsilateral side.

The decrease in the pupillary diameter was the result of interruption of

sympathetic fibers running through the trigeminal nerve to the eye. This was verified: (i) by lack of pupillary dilatation after instillation of cocaine (4 per cent) in the conjunctival sac; (ii) by absence of pupillary dilatation but presence of piloerection on stimulating the ipsilateral cervical sympathetic chain; (iii) by marked pupillary dilatation following parenteral injection of adrenalin. The latter is a sensitization phenomenon in the pupillary dilator fibers denervated by the trigeminal nerve section. Lack of piloerection as part of the syndrome of sympathetic paralysis was not seen. These observations indicate that sympathetic fibers to the eye course from the carotid plexus by way of the first division of the trigeminal nerve.

Cervical sympathetic chain

Stimulation of the cervical sympathetic did not yield any visible contractions in ipsilaterally denervated facial muscles. Eserinization did not alter the situation. There was not the slightest evidence of the Rogowicz phenomenon[5] even at a period when the denervated muscles were most sensitive. Stimulation was carried out under ether or nembutal anesthesia in 6 monkeys; in 3 the stimulus was applied above the middle cervical ganglion, in one at the middle cervical ganglion and in 2 at the inferior cervical ganglion. The duration of the stimulus varied from 5 to 45 secs. and varied in intensity.

Resection of the middle and superior cervical ganglia, with the intervening sympathetic trunk, and of the stellate ganglion by the posterior approach did not affect the fright reaction. Combined section of the ipsilateral trigeminal roots with the entire cervical sympathetic chain still did not inhibit the contractions of the denervated muscles observed in fright or sudden effort. The signs of stellate ganglionectomy in addition to the typical Horner's syndrome were increase of skin temperature, redness and some swelling (vasodilatation), anhidrosis and piloparesis of the hand.

To ensure interruption of all nerves which may possibly exist in the vicinity of the denervated facial muscles the trigeminal, chorda tympani, part of pharyngeal plexus, superior laryngeal, hypoglossal nerves and the entire cervical sympathetic chain were resected and the carotid artery denuded on the side of the facial denervation. In addition the vagus nerve was avulsed from the jugular foramen while the spinal accessory nerve was crushed. These procedures, carried out in several stages on the same monkey, were without influence on the fright reaction.*

* The following operations were carried out in one of the monkeys (Ptosis series No. 28): (i) Dec. 15, 1937, Section of left trigeminal nerve in middle fossa; (ii) Dec. 22, 1937, Resection and crushing of left facial nerve trunk. Dec. 27, 1937, First appearance of the fright reaction in the denervated facial muscles; (iii) Jan. 6, 1938, Stimulation and resection of the left stellate ganglion; (iv) Jan. 13, 1938, Resection of left facial nerve scar and branches together with resection of left superior cervical ganglion and the greater part of the sympathetic trunk, carotid denudation, and resection of superior laryngeal nerve; (v) Feb. 23, 1938, Resection of the left facial nerve scar with stimulation and resection of left hypoglossal nerve, stimulation and avulsion of the vagus nerve trunk from jugular foramen, section of chorda tympani and branches of glossopharyngeal plexus, crushing and section of branches of glossopharyngeal and spinal accessory nerves, ligation and section of external maxillary artery; and finally (vi), Apr. 1938, resection of left facial nerve scar tissue.

The fright reaction could be obtained at all times so long as the muscles remained denervated. The *facial muscles* were kept denervated by repeated section of possibly regenerated nerves. The facial paralysis was always evident. Electrical reactions of the facial muscles were absent. The signs of trigeminal nerve section persisted for months and were manifest by corneal analgesia with areflexia, analgesia of the face and deviation of the jaw to the ipsilateral side.

The signs of cervical sympathetic paralysis were myosis, enophthalmos, pseudoptosis, anhidrosis, piloparesis, dilatation of the angular vein; increased skin temperature with redness, swelling, and anhidrosis of the hand also persisting for many months. In addition all these denervated sympathetic structures were found to be hypersensitive to adrenalin. The evidence for denervation of the tongue and trapezius muscles was found in their responsiveness to parenteral injections of acetylcholin. The chief sign of vagus nerve resection was hoarseness. Thus with all these cranial and cervical sympathetic nerves destroyed contractions in the paralyzed facial muscles could still be obtained after fright. At no time was there observed any reduction in degree of these fright contractions.

Discussion

The foregoing experiments indicate that the contractions in denervated muscles induced by fright or sudden effort are due to a chemical agent, and, unless one accepts the theory that the autonomic system is a syncitium,[6] the source of the chemical substance is not regional. The substance is formed not only locally but throughout the body. Under conditions of strong emotion or sudden effort the entire nervous system is vigorously activated. At the nerve endings acetylcholin may be formed in amounts larger than usual. A portion of the excess of the cholinergic agent, after being absorbed into the general circulation, would then reach and act upon the denervated muscle in question.

The concentration of acetylcholin when absorbed into the blood stream need not be large. In a monkey, weighing 2300 gms., contraction in denervated facial muscles was obtained by the injection into the saphenous vein of 0.2 cc. of a solution of 1:50,000 of acetylcholin in saline. This small amount was effective in causing a minimal visible contraction in the denervated facial muscles in the anesthetized (ether or nembutal), and uneserinized monkey. With eserine the amount of acetylcholin necessary to bring about a minimal contraction was less. After the factors of hydrolysis by the cholin esterase and dilution by the blood stream are taken into consideration, the concentration of acetylcholin reaching the denervated facial muscles must be at least 1×10^{-8} gms. per cc. of blood in non-eserinized and 1×10^{-9} or 1×10^{-10} in the eserinized monkey. Such sensitivity to acetylcholin is greater than some leech muscles possess. It would appear that the denervated facial muscle of monkeys is a better indicator for acetylcholin than the leech.

Thus far attempts to recover acetylcholin from the blood stream of frightened monkeys have been fruitless. To obtain sufficient volumes of blood

from active monkeys is difficult and to detect such small amounts of acetylcholin even by the eserinized leech muscle is a procedure fraught with difficulty.

Summary

1. The fright reaction (contractions in denervated facial or ocular muscles induced by fright) was neither abolished nor diminished by resection of combinations of nerves, from the third to the twelfth cranial nerves inclusive, and by simultaneous extirpation of the entire ipsilateral cervical sympathetic chain.

2. These findings exclude the possibility that the fright reaction is due to a local secretion of acetylcholin. The effect is probably due to a general secretion of acetylcholin-like substance with secondary diffusion through the blood stream.

3. Intravenous injections of acetylcholin in the uneserinized monkey were effective in causing contractions in denervated muscles in concentrations less than 1×10^{-9}. Such small amounts of acetylcholin would be technically difficult to recover from blood.

4. Intracranial section of the trigeminal nerve caused the ipsilateral pupillary dilator fibers to be sensitive to adrenalin.

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FUNCTIONAL ORGANIZATION IN THE FACE-SUBDIVISION OF THE SENSORY CORTEX OF THE MONKEY (*MACACA MULATTA*)*

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(Received for publication June 23, 1938)

INTRODUCTION

ON LOCAL strychninization, *i.e.*, the strychninization of only a few (1–4) square millimeters, of any portion of the cerebral cortex a typical change in the electrocorticogram (ECG) occurs, namely the temporary appearance of large, rapid potential-fluctuations, or "strychnine-spikes." In some regions of the cortex, for instance in the visual cortex, this change remains local, in others the hyperactivity induced by the strychnine does not remain confined to the strychninized locus, but spreads. This is especially conspicuous in the sensorimotor cortex. Upon local strychninization of almost any constituent area of this region of the cortex, strychnine-spikes appear in the ECG not only at the site of strychninization, but over the entire area and even in other areas.[1]

The areal distribution of these spikes differs with each area locally strychninized, thus revealing details of functional organization, *i.e.*, specifically directed functional (and obviously anatomical) relations, in the sensorimotor cortex. The paper just quoted presented the functional organization in the leg- and arm-subdivisions of the sensorimotor cortex; the present paper deals with a similar investigation of the face-subdivision of this region.

METHODS

All experiments were performed on monkeys (*Macaca mulatta*), fully anaesthetized with Dial;** 0.45 cc. per kilogram bodyweight, half of the dose given intraperitoneally, half of it intramuscularly.

For the electrophysiological and other methodological details the reader is referred to the paper on the functional organization in the leg- and arm-subdivsions in the sensorimotor cortex.[1]

The problem of the placing of the electrodes and the strychnine presents peculiar difficulties in the face-subdivision. The number of areas in this region, especially in its precentral portion, is relatively large. The variability of the macaque's brain is considerable and, finally, worst of all, the boundaries between many of the constituent areas of this subdivision are not indicated by any external landmarks. For want of a cytoarchitectonic map of the macaque's brain, the extent and location of its sensory cortex[2] is given in Fig. 1, in which the areas of the Vogts' map of the cercopitheque's brain (slightly modified) are indicated. It was assumed for this investigation that the cytoarchitecture of the macaque's cortex resembles that of the cercopitheque's brain. The diagram of the Vogts probably represents an "average" picture of their findings in several animals, for they state that their map is based on the study of more than 100 brains of cercopitheque monkeys, but "dass wir uns (aber) in den Abgrenzungen der einzelnen Felder an bestimmte, günstig geschnittene und die Grenzen besonders deutlich zeigende Präparate gehalten haben",[3] (p. 371). Their diagram for the cercopitheque's brain differs in some respects from the macaque's brain, especially in the shape of the arcuate sulcus. This factor and particularly

* The expenses of this investigation were defrayed by a grant from the Fluid Research Funds of the Yale University School of Medicine.

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** The Dial was kindly put at our disposal by the Ciba Company.

the absence of external landmarks for many of the areal boundaries makes experiments in this region of the cortex of the kind presented in this paper rather difficult. Only analytical comparison of the configuration of the brains and careful correlation of the results of many experiments can help out here.

Results

For the orientation of the reader with respect to the placing of the electrodes and the strychnine in these experiments the map mentioned in the introduction is given in Fig. 1. Attention should be called to the inclusion of areas L.4-s, A.4-s and F.4-s.

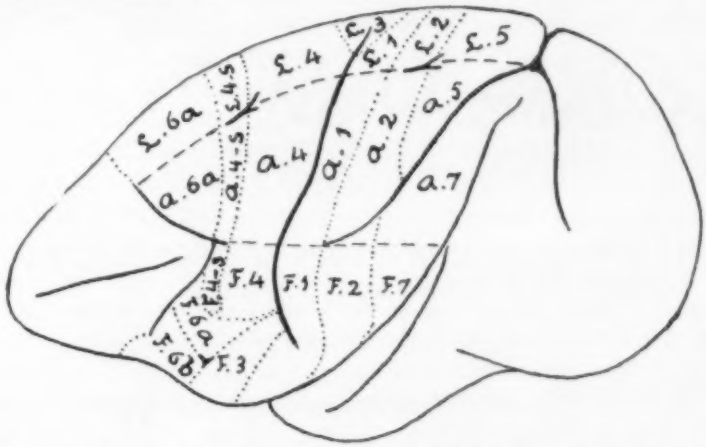

Fig. 1. Sensory cortex of *Macaca mulatta* with the architectonic areas (modified) of the map of the cercopitheque's brain after C. and O. Vogt. The deviations from their diagram are: 1. the introduction of the areas L.4-s, A.4-s and F.4-s, 2. the omission of the subdivisions of F.6b, F.3, L.6a and A.6a. It should be noted that these modifications are based upon consideration of physiological, not anatomical evidence.

I. *F.6b.*
   a. *F.6bβ.* Local strychninization of F.6bβ "fires" this area, and possibly F.3, but not F.6bα, F.6a, F.4, F.1 or F.2.
   b. *F.6bα.* Attempts to strychninize this area either produced results like those obtained upon strychninization of F.6bβ or those following strychninization of F.6a (see below sub II), with "firing" of F.6bα in both cases.

II. *F.6a.*
   Local strychninization of F.6a "fires" itself and F.4 to a less extent (*i.e.* with few and small spikes) and F.3, but not F.6b, F.1 F.2.

III. *F.4-s.*
   Local strychninization of the anterior margin of F.4 results in a temporary suppression of the electrical activity of F.4. (See Fig. 2).

IV. *F.4.*
   Local strychninization of F.4 "fires" itself, F.6a, F.1 and to a less extent F.3, but not F.6b or F.2. In Fig. 3 is shown the temporary "firing" of F.4 and F.1 following local strychninization of F.4.

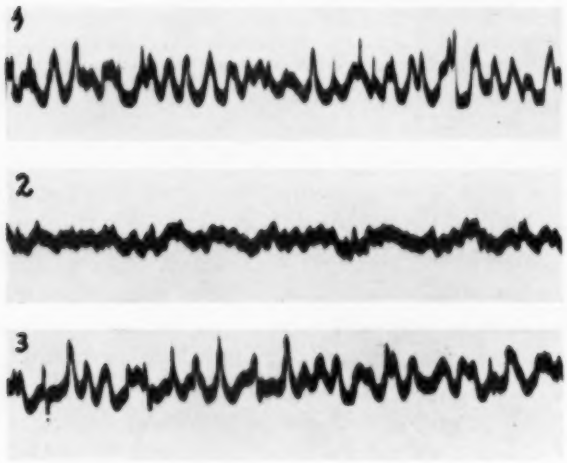

FIG. 2. Shows the temporary suppression of the electrical activity of F.4 following local strychninization of F.4-s. Record 1: before, record 2: at the height of suppression 11 minutes after this strychninization, and record 3: 3 minutes later showing the return of activity.

V. *F.3.*
Local strychninization of this area "fires" itself, F.6a and to a less extent F.1, but not F.6b, F.4 or F.2.

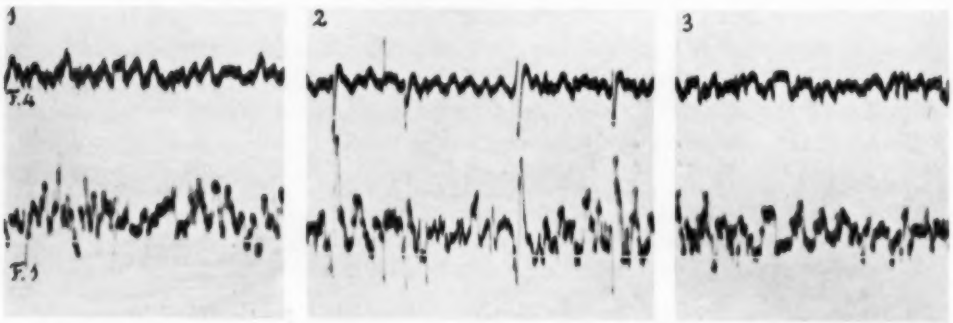

FIG. 3. Shows the temporary firing of F.4 and F.1 following local strychninization of F.4. Record 1: control; record 2: height of "firing" 5 minutes after the strychninization; record 3: return to "normal" 23 minutes later.

VI. *F.1.*
Local strychninization of the postcentral portion of F.1 "fires" itself and to a less extent F.6a. It suppresses the activity of F.4 and it fails to "fire" F.6b and F.2. In some experiments a mixed picture of suppression with little spikes appeared in the electrocorticogram of F.4. In one experiment local strychninization of F.1 resulted in a "firing" of F.4 without obvious suppression.

VII. *F.2.*
Local strychninization of this area "fires" itself and F.1 (postcentral portion), it fails to "fire" F.6b, F.6a, F.4 and F.3.

VIII. *F.7.*
Local strychninization of F.7 "fires" itself, F.2 and to a less extent F.1, while it fails to "fire" F.4, F.3, F.6a and F.6b.

Discussion

Any experimentation requiring differentiation within the face-subdivision of the sensorimotor cortex is difficult for want of external landmarks between its constituent cytoarchitectonic areas. Thus it is impossible to know with certainty beforehand whether the strychninization or the pick-up electrodes are in each case confined to one particular area. Furthermore the individual variation in this subdivision is so great that to know where the areal boundaries are in one animal does not help much in the next. Worst of all is the variation at the triple-point, where F.6a, F.6b and F.3 meet. This point is sometimes, as in the diagram of the Vogts, marked by a shallow dimple, in other animals there is no marking, in still others there is a definite, long anterior subcentral sulcus, usually, but not always, parallel to the fissura centralis. No cytoarchitectonic maps covering all these and other variations exist. Therefore, in each animal several strychninizations and several electrocorticograms from neighbouring loci are required in this region to obtain discrete results, for any one strychninization may be so performed or any pair of electrodes may be so placed as unwittingly to cross a boundary between two areas. Because the local strychninization of each of the three areas meeting at the triple-point results in the firing of a unique group of areas, it is ultimately possible to distinguish the strychninization of any one of these areas from that of any combination of them. Only in the case of area F.6bα have we been unable to apply this diagnostic procedure, for all attempts to strychninize it always resulted in pictures indistinguishable from those which would have been produced if one or the other of the adjacent areas, F.6bβ or F.6aα, had been involved.

One of the major results in these experiments is that there exists a continuation of the "strip," our L.4-s and A.4-s, into the face-subdivision, *i.e.*, that there exists a F.4-s. This area is a very narrow strip of cortex, 1 to 1.5 mm. wide, 5 to 6 mm. long, lying behind and usually tangent to the upper portion of the inferior ramus of the arcuate sulcus. Its lower end is separated from the arcuate sulcus by a wedge of cortex whose properties resemble those of F.6a (see Fig. 1). In one animal F.4-s nowhere touched the arcuate sulcus, being separated from it by a narrow band of cortex, ca 1.5 mm. wide, which "behaved" like F.6a.

Another striking result in these experiments is the observation that, whereas L.6a and A.6a are not fired by any other area of the leg- and arm-subdivisions, F.6a is fired by F.4, F.3 and to a less extent by F.1. Moreover, whereas strychninization of L.6a or A.6a "fires" the whole of the leg- and arm-subdivision, both pre- and postcentral, the strychninization of F.6a not only "fires" no area outside the face-subdivision, but also fails to "fire" its own postcentral portion and F.6b.

As for F.6b, while not "fired" by any other area, thus resembling L.6a and A.6a, its failure to "fire" any other area, leaves it unique in the sensorimotor cortex. The mixed picture in F.4 obtained upon strychninization of F.1 and the failure of F.2 to "fire" F.4 needs a few words. In the arm- and leg-subdivisions early attempts to strychninize L.1 or A.1 resulted sometimes in

these mixed pictures in L.4 or A.4. We later learned that the mixture was due to trespassing with the strychnine onto area 2. The same explanation may obtain for the experiments on F.1, but it would imply that in several animals (3 out of 6) F.1 was narrower than indicated by the diagram of the Vogts. The one experiment in which strychninization of F.1 resulted in a definite "firing" of F.4 and failed to "fire" F.6a stands alone and must remain unexplained for the present.

One last observation should be mentioned. In several experiments pick-up electrodes were put on F.4, A.4 and L.4 and strychnine applied locally to L.4-s, A.4-s and F.4-s seriatim. As stated previously, strychninization of L.4-s or A.4-s resulted in a temporary suppression of the activity of L.4 and A.4, without any change in the ECG of F.4. The strychninization of F.4-s not only suppressed the activity of F.4, but also to a less extent that of A.4, while the ECG of L.4 remained unchanged. This finding indicates the existence of a one-way functional relation between F.4-s and A.4. This is of special interest because in all the experiments of this series the "firing" was confined to areas of the subdivision locally strychninized, *i.e.*, to areas of the face-region. Therefore, the suppression of the electrical activity of A.4 upon local strychninization of F.4-s is the only instance in which the functional boundary between the face- and arm-subdivisions of the sensorimotor cortex is not respected. If the suppression from F.4-s like that of L.4-s and A.4-s occurs via subcortical structures and not along cortico-cortical pathways, this transgression of the functional boundary between the face- and arm-subdivisions of the sensorimotor cortex is not a transgression of this functional boundary at the cortical level. This leaves the lack of functional boundary between L.6a and A.6a and L.4-s and A.4-s mentioned previously (1, pp. 73–74 and 82–83) as the only demonstrated hiatus *at the cortical level* in the functional boundaries between the various subdivisions of the sensorimotor cortex.

Summary

1. By combination of local strychninization and recording of the electrograms of various areas of the sensorimotor cortex, the functional organization of the face-subdivision of this region was investigated.

2. As previously in the leg- and arm-subdivisions, these experiments revealed directed functional relations between the various constituent areas of the face-subdivision.

3. No "firing" of any area of the arm-subdivision was found upon local strychninization of any area of the face-region.

4. Local strychninization of two areas, namely F.4-s and F.1 (postcentral), temporarily suppressed the electrical activity of F.4.

5. Local strychninization of F.4-s suppressed to a less extent also the electrical activity of A.4. This is the only instance encountered in which strychninization within the face-subdivision produced any change in another subdivision.

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PATHWAYS THROUGH THE SYMPATHETIC NERVOUS SYSTEM IN THE BULLFROG*

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(Received for publication June 24, 1938)

PROMPTED by certain difficulties of interpretation in physiological experiments on the splanchnic nerve of the bullfrog (Bishop, 1937), we have undertaken a detailed anatomical survey of the frog sympathetic system. This paper deals with the portion of this system which arises from the first six nerve levels, and includes the supply to the mesentery and gut. The course of each major bundle of pre-ganglionic fibers has been traced, its region of synapse located, and the course of its post-ganglionic fibers determined in general. The methods employed have been dissection, reconstruction from sections of normal and of partially degenerated preparations, and recording of action potentials by means of the oscillograph. Stimulation of nerves in the body has indicated the ultimate destination and function of certain of the pathways recognizable in the sympathetic rami and trunks. Twenty-five bullfrogs have been employed, from which over sixty blocks of tissue have been reconstructed from sections. These include five of the 2nd and 3rd nerve levels, eight of the 4th, eighteen of the 5th, twelve of the 6th, three of the 7th, and ten of the coeliac ganglion region.

From these preparations, an anatomical and functional pattern emerges which, in spite of considerable variability from one animal to another, is rather diagrammatic in its essential relationships (Fig. 1). Considering the most anterior spinal nerve present in the adult as the second segmental nerve, this nerve connects with the sympathetic trunk usually by one or two very fine rami. The 3rd nerve sends one or more rami into it, and receives at least one bundle from it. The 4th nerve sends a ramus anteriorly toward the 3rd, and another posteriorly toward the 5th, and receives two rami from the sympathetic trunk. The 5th nerve contributes two rami, and receives two. The 6th contributes one ramus, chiefly to the posterior sympathetic trunk, and receives one. The 7th nerve contributes one ramus to the trunk, and receives one. Its fibers do not enter the splanchnic nerve, but a strand from the seventh ganglion may pass to the dorsal aorta and kidney.

The pattern is made more obvious when the synaptic regions are taken into account. With a few exceptions to be noted, (i) a ramus passing *to* the sympathetic does not synapse in the ganglion of that level, but in ganglia anterior and posterior to it; (ii) the rami passing *from* the sympathetic to the peripheral spinal nerves arise from ganglia at the levels of these respective nerves; (iii) the components of the splanchnic nerve arise mainly from the third to the

* This work has been supported in part by a grant from the Rockefeller Foundation (to G.H.B.) for research in neurophysiology, and in part by a grant from the Committee on Scientific Research of the American Medical Association (to J.O'L.).

sixth rami, and each synapses partly in the ganglion at the level next below it, and partly in the coeliac ganglion, or even in ganglia more peripheral along the sympathetic nerves.

There are thus two histologically recognizable components from each level: one passing to the peripheral nerves, and one to the viscera. At the 4th level there may be two separate ganglia, one giving rise to the rami passing peripherally in the 4th nerve, the other containing the synapses of 3rd nerve fibers whose post-ganglionic fibers pass into the splanchnic nerve.

The terms "white" and "grey" rami will be employed as usual to designate pre-ganglionic and post-ganglionic connections, respectively, between the spinal nerves and the sympathetic trunk, with the reservation that they cannot be differentiated in the frog by their color. In fact, the "grey" rami of the 3rd to 6th nerves are preponderantly myelinated, while the "white" rami contain many non-myelinated fibers. The histological and physiological results can be correlated through the fact that the myelinated fibers of the sympathetic have a lower threshold and a faster conduction rate than the non-myelinated. They give rise to a *B* wave, and the fastest of these fibers conduct at about $2\frac{1}{2}$ m.p.s. in excised preparations at room temperature. The non-myelinated fibers give rise to a *C* wave, and the fastest of them conduct at about $\frac{1}{2}$ m.p.s. The two potential waves appearing when such fibers are stimulated are well separated after 10 mm. conduction. Besides these two groups of fibers, a variable number of sensory myelinated fibers course through the sympathetic; these conduct more rapidly, and the potential to which they give rise appears ahead of the sympathetic *B* wave, in the position of the γ or δ component of the *A* wave of the sciatic.

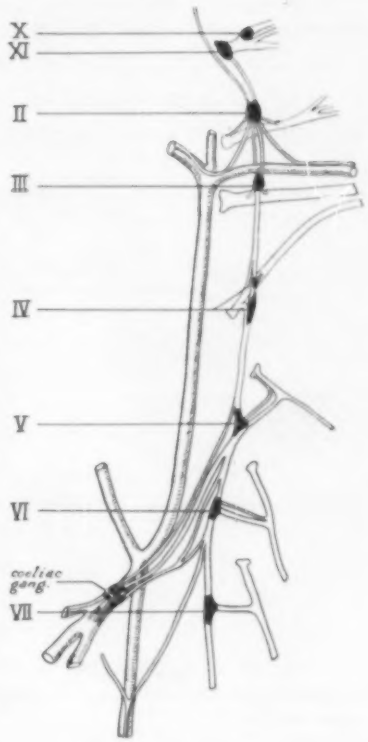


FIG. 1. Schematic diagram of the sympathetic supply to the splanchnic nerve of the bullfrog. Sympathetic chain ganglia numbered II to VII.

TECHNIQUE

Bullfrogs were operated under local anaesthesia through a ventral incision to the left of the midline. Either arch of the aorta could be deflected laterally, and after cutting through the dorsal peritoneum, roots were cut by an incision with an iris knife medial to the dorsal root ganglion. Sympathetic trunks and rami were completely severed with scissors. All operations were checked by sections after degeneration from two to five months in the laboratory at room temperature. In physiological experiments, conduction pathways were traced by oscillographic recording, and contractions of blood vessels and of the gut

were observed after stimulation at various regions. Nerves were then fixed in 10 per cent formol, 5 per cent glacial acetic, stained by osmic acid or silver (usually the Bodian (1936) technique as modified by H. A. Davenport), and cut in 7 to 10μ sections. After one or two months, degenerating myelinated fibers are clearly detectable in osmic, but not in silver; that is, the sheaths are altered but the axons are still intact. After about five months, fiber bundles are grossly shrunken and the axons disappear. Reconstruction $\times 80$ were made of sectioned nerves by counting the serial sections and drawing certain of them in camera lucida. In the figures, areas of ganglion cells are shaded. In making these drawings, the fascicles of complex nerves are represented as lying in a plane, which distorts somewhat their natural relationships.

4TH NERVE LEVEL

The relationships of the 4th nerve level will be discussed first because they illustrate most diagrammatically the courses of typical pathways (Figs. 2–6). The 4th nerve runs anteriorly and laterally to join the brachial plexus (N_{IV}), and is crossed by the sympathetic trunk at an angle of about 30° approximately 3 mm. from the dorsal root ganglion. Posterior to this contact, however, a large white ramus turns caudad from the 4th nerve and joins the sympathetic (W_p). A triangle is thus formed with the sympathetic as the base and the white ramus and the 4th nerve as two sides. Just anterior to the junction of trunk and ramus, the main 4th sympathetic ganglion lies on the trunk (G_{IV}), but no 4th white ramus fibers enter it. Anterior to this, and just posterior to the crossing of the 4th nerve, the two grey rami for the 4th nerve (G) arise from the main sympathetic ganglion or from small separate ganglia. Their post-ganglionic fibers are preponderantly myelinated. At about the same level, one or more white rami pass from the 4th nerve to the sympathetic (W_a), where they ascend in fiber tracts which pass by the 4th ganglia without

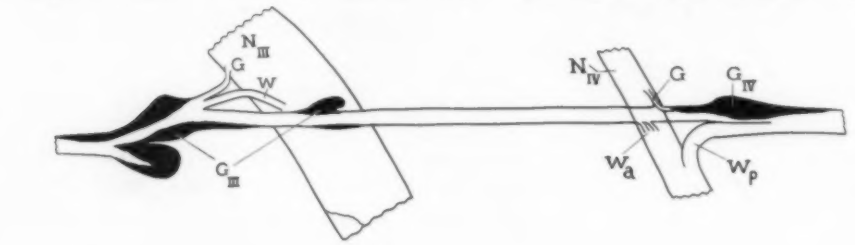
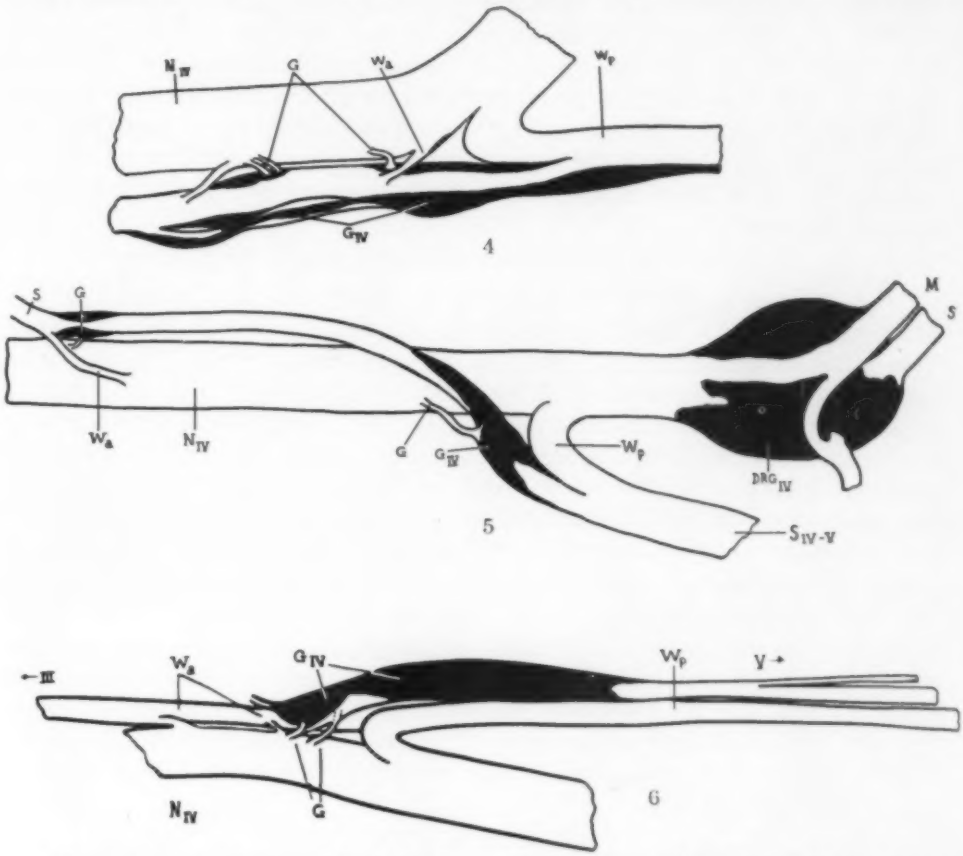


FIG. 2. Reconstruction of 3rd and 4th levels of the sympathetic chain. N, spinal nerve, G, grey ramus, W_a, white ramus anterior, W_p, white ramus posterior, G_{III} etc., chain ganglia shaded.

FIG. 3. Legends as in 2. Multiple ganglionic masses along sympathetic, and diagrammatic division of 4th white ramus into ascending and descending branches, neither of which terminates at synapses of this level.

synapses. Thus, few if any white ramus fibers from the 4th level synapse in ganglia at that level, but the grey rami obviously have done so in large part.

The 4th white ramus coursing posteriorly fuses with the trunk from the 3rd level, usually well below the 4th ganglia, to form a single bundle. Some of these 4th white ramus fibers synapse in the 5th ganglion, their post-ganglionic fibers forming the two 5th grey rami. In many preparations, a branch of the



FIGS. 4, 5, 6. 4th sympathetic level. *4* and *5* appear to have separate grey ramus ganglia. In *5*, the motor component passes through the dorsal root ganglion and emerges in the trunk on the side opposite the white ramus, and a majority of the white ramus fibers can be traced to the ganglionic region. In *6*, the descending white ramus is separate from the 4th sympathetic ganglion.

sympathetic trunk, containing from one-third to two-thirds of the trunk fibers, the number varying in different preparations, passes the 5th and 6th ganglia entirely in a separate strand, which remains separate until it reaches the region of the coeliac ganglion or, in some preparations, rejoins the main nerve. Some of these fibers are obviously those from the 3rd level which have synapsed in the 4th ganglion; there may be some pre-ganglionic fibers from the 3rd and 4th levels which synapse in the coeliac ganglion. The 4th descend-

ing white ramus (W_p) contributes about half the fibers coursing between the 4th and 5th levels.

The 4th ascending white ramus (W_a) also consists of two components, one passing to the 3rd nerve grey rami and one to the 2nd and 3rd ganglia, from the former of which several strands supply the head, heart, vessels, etc. In two cases a fine ramus has been found from the 4th nerve parallel to but separate from the sympathetic trunk, ending in a small ganglion, from which two rami entered the 3rd nerve. No other grey rami were found to the 3rd nerves in these preparations, and this fine white ramus contained about one-fourth of the total bulk ascending in the sympathetic from the 4th level. It may be estimated, therefore, that something like three-fourths of the ascending 4th ramus fibers contribute to the supply of the head and heart region. The ascending 4th nerve fibers compose a little less than one-half the total between 3rd and 4th levels.*

IInd and IIIrd Nerve Levels

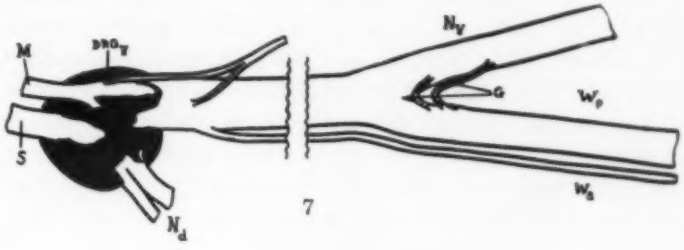
The 2nd nerve usually receives no grey rami from the sympathetic (one preparation has contained a grey ramus), but sends a very fine white ramus from close to its dorsal root ganglion to the 2nd ganglion. The 3rd level sometimes appears to contain no sympathetic ganglion in the frog, but we have found a variable number, from none to four (Figs. 2 and 3), strung along the sympathetic trunk in this region. When no ganglia are present in the immediate vicinity of the 3rd nerve, both white and grey rami pass to the 2nd ganglion, which in this case therefore must represent a fusion of the 2nd ganglion with the 3rd. Contrary to the picture at the 4th level, white rami as well as grey appear always to pass immediately to regions of ganglion cells, and those supplying the head region presumably synapse in the 2nd and 3rd ganglia.Those supplying the posterior regions of the body may also synapse there in part, for the bulk of the sympathetic trunk between 3rd and 4th levels, subtracting the ascending 4th white rami, is still considerably larger than the bulk of the 3rd white ramus. Many of the 3rd nerve fibers, however, synapse in the main 4th ganglion, and stimulation of these causes contraction of the stomach.

5th Nerve Level

The main 5th white ramus (Figs. 7–10, W_p) contributes more than one-half the fibers of the splanchnic nerve. Its size is about equal to that of the 5th

* In this and the following accounts, the statements must be taken generally, for many striking variations are found. For instance, in one preparation with 4th nerve and sympathetic cut anterior to the 4th spinal level, and the 5th white rami cut, there was inappreciable degeneration between 4th and 5th sympathetic ganglia, or even in the stub of nerve anterior to the 4th ganglion. Above the cut the sympathetic trunk to the 3rd level was completely degenerated. Both 4th and 5th sympathetic ganglia were very small, consisting only of scattered cells, and presumably supplied chiefly the grey rami to these levels. In this case no component from above the 4th level passed to the splanchnic nerve; and the sympathetic trunk between 5th and 4th levels, exclusive of the 4th white ramus, must have consisted chiefly of ascending fibers from below the 5th level passing to the 2nd and 3rd levels. The 3rd nerve white ramus passed anteriorly toward the 2nd ganglion, and the 3rd grey ramus was not degenerated, apparently arising from the 3rd sympathetic ganglion.

spinal nerve (N_V) with which it forms the 5th trunk. The two grey rami are usually combined with it, but sometimes separate out as individual strands



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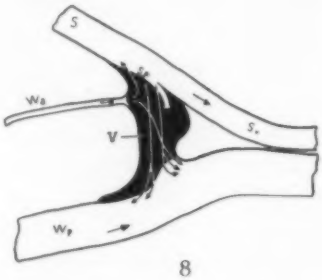

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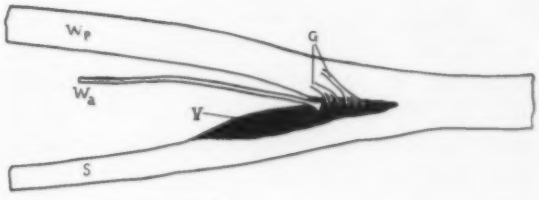

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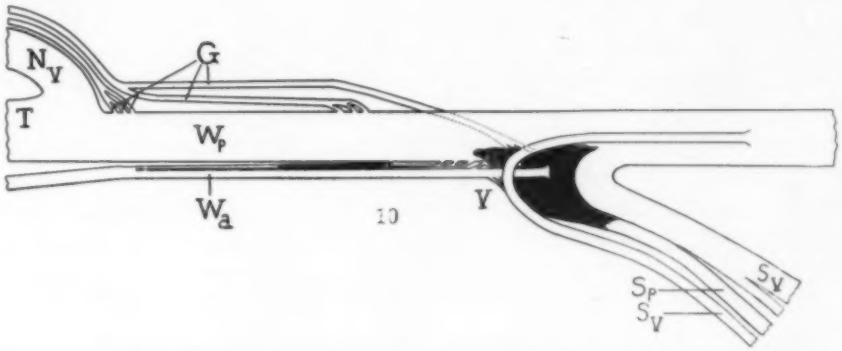

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FIG. 7. 5th dorsal root ganglion and division of 5th nerve and white ramus. Roots degenerated, white rami show only slight degeneration, *i.e.*, the majority of the fibers come from the spinal ganglion. Stimulation of ramus caused gut contraction. Degenerated motor root component mixes with sensory component only below branching of small white ramus W_a.

FIGS. 8, 9, 10. 5th sympathetic ganglia, showing relation of sympathetic trunk and white rami. S_v, visceral branch of anterior sympathetic trunk by-passing 5th and 6th ganglia as separate strand to coeliac region in *9*, joining trunk again in *10*. The 5th nerve and sympathetic trunk in *10* were drawn apart in directions opposite to their normal relations before fixation.

nears its junction with the 5th nerve (Fig. 10). These can always be detected in sections at this crotch by the fact that they are cut longitudinally as they pass from ramus to nerve. They can usually be recognized at the crotch of the

sympathetic ganglion. In two series of sections they have been traced throughout the length of the white ramus, recognizable by a preponderance of myelinated fibers but otherwise appearing merely as two fascicles among the many of which the ramus is composed, without anatomical demarcation from the rest. They arise wholly from the 5th sympathetic ganglion, with their pre-ganglionic fibers wholly in the anterior sympathetic trunk, the stimulation of which produces a *B* wave, but no detectable *C* wave in the 5th nerve (Bishop, 1937). In some osmicated sections, a few structures which stain faintly appear to be non-myelinated fibers, but whether there are more than could be accounted for as sections through nodes of Ranvier has not been determined.

A second fine white ramus separates from the 5th trunk (W_a), usually just below the dorsal root ganglion but always above the separation of 5th nerve and ramus. It contains 20 to 40 myelinated fibers, and at least twice that many non-myelinated. It runs parallel to the main white ramus on the side opposite the 5th nerve, and enters the 5th sympathetic ganglion. Its fibers can be traced by stimulation of the 5th trunk after cutting the main white ramus below the point of stimulation. A *B* and a *C* wave then appear in the splanchnic peripheral to the 5th sympathetic ganglion, of a few microvolts each, when the *C* wave produced by stimulation of the uncut larger ramus is $\frac{1}{2}$ millivolt. *A B* wave only, of some 10 microvolts amplitude, appears also in the anterior sympathetic trunk. No conduction takes place in the reverse direction, or a much smaller *C* wave may appear. The amplitudes of the post-ganglionic waves recorded are such as to indicate that each pre-ganglionic fiber in this ramus must synapse with a number of post-ganglionic neurons. No detectable effect on the musculature of intestine or mesenteric vessels has been observed from stimulation of these fibers, in preparations where stimulation of the main 5th white ramus caused massive contraction of stomach and gut and stoppage of flow through mesenteric vessels. The destination of the fibers ascending in the anterior sympathetic trunk is partly to the 3rd, partly to the 4th grey rami.

The sympathetic often divides just anterior to the 5th sympathetic ganglion (Figs. 7 and 10), and then one branch only enters the ganglion. The ganglion is variable in size, and in some cases its cells would seem to be sufficient in number only to supply the two components shown to synapse there, the fine 5th white ramus and the anterior sympathetic pre-ganglionic fibers for the 5th grey rami. In other cases, a larger ganglion must contain synapses of anterior sympathetic fibers whose post-ganglionics course in the splanchnic nerve and posterior sympathetic trunk. When the sympathetic divides above the ganglion, the strand which joins the 5th rami at this ganglion varies in size with the size of the ganglion. The splanchnic components from the 5th ganglion and white ramus form a single trunk, in which, however, most of the main white ramus fibers from the 5th level can be followed past the ganglion without passing through regions containing ganglion cells. When there is a separate strand from the anterior sympathetic past the 5th ganglion, it may

not fuse with this trunk, although it may have minor anastomoses with it; but few if any of the fibers which have by-passed the 5th ganglion enter the 6th ganglion or posterior sympathetic trunk.

Below the 5th sympathetic ganglion, then, the splanchnic-sympathetic consists typically of two strands (Figs. 7, 11 and 12); if the anterior sympathetic has not divided above the 5th ganglion, a corresponding division takes

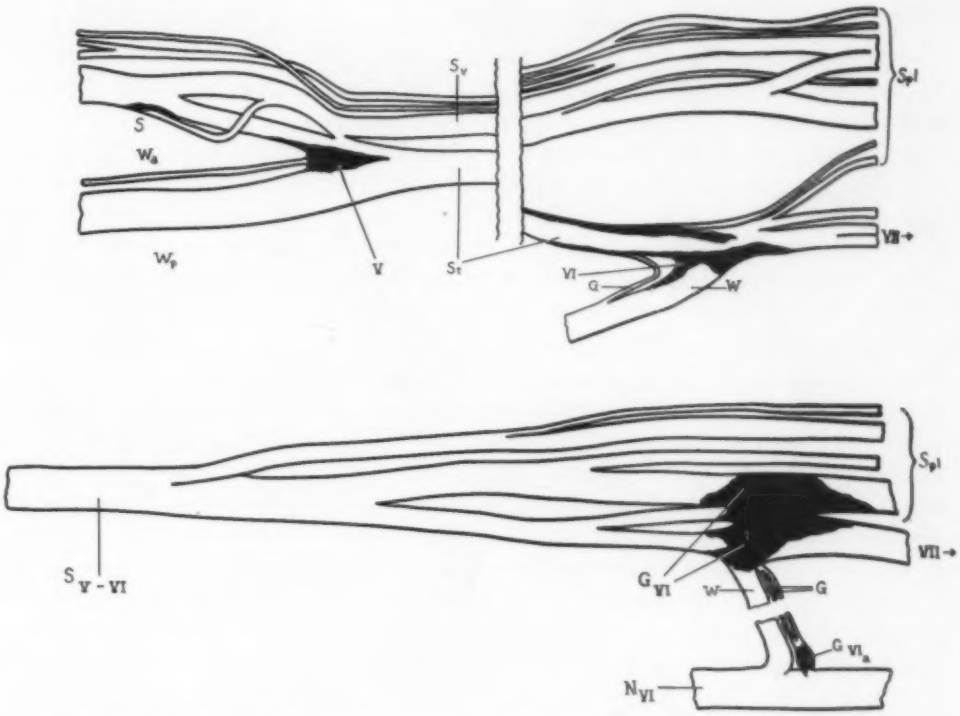

FIG. 11. Regions of 5th and 6th sympathetic ganglia. S_v, strand of anterior sympathetic trunk by-passing 5th and 6th ganglia on way to coeliac. S_t, sympathetic trunk. S_{pl} splanchnic components.

FIG. 12. 6th ganglion not only on sympathetic trunk, but also on strand that passes from 5th ramus and ganglion to splanchnic. It presumably represents a functional component of the coeliac ganglion, G_{VI_a} is a separate grey ramus ganglion at the junction of grey ramus and 6th nerve instead of at the usual position on the sympathetic trunk.

place just below it, and one strand carries chiefly anterior sympathetic fibers to the viscera. The remaining anterior sympathetic-5th white ramus bundle further separates into three main parts, each of which may divide into smaller strands, to form a plexus. The largest component passes to the coeliac ganglion. The smallest fascicle also passes to this ganglion, and may receive a fine strand from below the 6th ganglion, which then must carry the only contribution from the 6th ramus to the splanchnic. The middle-sized strand runs to the 6th ganglion, beyond which it divides further into two parts.

The larger of these is the posterior sympathetic trunk, the smaller passes along the dorsal aorta and probably supplies the kidney but not the gut, except in those cases where a strand is given off, as mentioned above, to the smaller of the splanchnic divisions. This strand, from the 6th ganglion region to the splanchnic, is relatively much larger in the greenfrog than in the bullfrog.

6TH NERVE LEVEL

The 6th level has two rami, one grey and one white, often fused to a common bundle (Figs. 11 and 12). In one case two ganglionic masses corresponded to the junctions of these two rami with the sympathetic, in which case one was presumably a distinct grey ramus ganglion (see 4th ganglion, above). In another case, a fine ramus passed from near the 6th sympathetic ganglion to a small grey ramus ganglion at the junction of the 6th white ramus with the 6th spinal nerve (G_{VIa}, Fig. 12). These fibers, presumably pre-ganglionic, came from the direction of the 5th level. Such displacement of ganglionic masses from their conventional positions emphasizes the anatomical distinctness of the spinal and visceral components of the sympathetic.

The 6th sympathetic ganglion lies on that division of the sympathetic-5th ramus trunk which also contains the 5th ganglion (Fig. 11). Most of its post-ganglionic fibers pass into the posterior sympathetic trunk, the other divisions of the splanchnic containing no ganglion cells. In two cases, however, a ganglion has been found on the larger of the three divisions as well (Fig. 12, G_{VI}), whose post-ganglionic fibers passed into the splanchnic. The pre-ganglionics apparently came from the 5th white ramus. This anomalously situated ganglion then represents functionally a portion of the coeliac ganglion. Since, however, some of the fibers from the 4th level typically synapse in the 5th ganglion on their way to the splanchnic, while others synapse in the coeliac, this extra 6th ganglionic mass bears the same relation to the 5th white ramus as the 5th ganglion does to the 4th descending ramus. In the usual case, few fibers in this strand from the 5th white ramus snyapse before they reach the coeliac ganglion. In some cases, few fibers from the anterior sympathetic trunk synapse in the 5th ganglion on their way to the splanchnic. It follows that the marked variability in the sizes of the 5th and 6th ganglia must be an anatomical variation rather than a functional one, and that those portions of the 4th, 5th, and 6th ganglia which correspond to the visceral components of the sympathetic are functionally identical with the coeliac ganglion. The coeliac ganglion can conversely be looked upon as consisting of portions of the 4th, 5th, and 6th sympathetic ganglia which have migrated distally to a position away from the sympathetic trunk, on the splanchnic nerve.

7TH NERVE LEVEL

The arrangement of the 7th level is essentially like that of the 6th, a strand from the 7th ganglion to the dorsal aorta corresponding to the strand from the 6th which divides to dorsal aorta and splanchnic.

The Coeliac Ganglion

In some frogs no coeliac ganglion can be found, a few scattered cells occurring along the strands of a plexus around the coeliac artery. At the other extreme the ganglion consists of a large compact mass of cells on each of the three main fascicles entering from each side of the body, with smaller ganglionic masses on the finer strands of the plexus. All variations occur between these extremes. In several cases individual strands could be traced through this region along which no cells were found, while other strands had well-formed ganglionic masses. The size of the coeliac ganglion could not be correlated with the sizes of the sympathetic ganglia in the same preparation, as might have been expected if the coeliac ganglion represented parts of these other ganglia transported peripherally. Since it has been reported (Ecker and Wiedersheim, 1896) that in the greenfrog, ganglion cells and small ganglia may be scattered along the branches of the splanchnic nerve near their termination in the viscera, it may be inferred that when not present in its conventional location, the coeliac ganglion may be represented by such scattered ganglionic masses, as well as by masses of cells at the 4th, 5th, and 6th sympathetic levels, as suggested above.

When a well-formed ganglion is present, the coeliac plexus in which it is located shows a certain structural pattern related to it. The strands may anastomose and divide, but previously to entering the ganglion, a specific anastomosis occurs between the nerves from the two sides of the body. This anastomosis lies on the posterior surface of the artery, and is a pre-ganglionic one in the sense that distal to the junction of the strands from either side the common strand may contain many ganglion cells. This junction definitely involves a chiasma. From this mass a strand of fibers leaves on either side to accompany the dorsal aorta, the remainder mixes with the rest of the plexus, On the anterior surface of the artery, and distal to the ganglion, a second or post-ganglionic anastomosis occurs, from which arise several main branches of the splanchnic nerve. One or more branches arise from either side of the remaining mass whose fibers appear not to have crossed the midline. The result is effectively a ring of ganglionic tissue encircling the coeliac artery, the axis of the ring at an angle to the axis of the artery, the branches of the splanchnic leaving from the periphery of the ring along its distal margin.

Physiological Implications

This histological work was undertaken in the hope of clarifying a situation reported on previously (Lucas and Miksecek, 1936; Bishop, 1937), that many fibers originating in the dorsal root ganglia of the bullfrog, but without central connections detectable in either root, produced when stimulated a massive contraction of the stomach and gut. On many of the frogs of the present series, experiments were performed similar to previous experiments on intact undegenerated preparations. The results were consistent with previous findings, and certain more specific information was obtained, although no explanation of the normal action of these fibers has been arrived at.

Myelination. It can be stated definitely that in the frog sympathetic many post-ganglionic fibers are myelinated, that certain grey rami to the somatic nerves are chiefly myelinated, and that their pre-ganglionic fibers are similarly myelinated. In the 5th ganglion, myelinated pre-ganglionics apparently synapse with both myelinated and non-myelinated post-ganglionics, judging by the general appearance of the fascicles in favorably distributed plexuses, without detailed fiber counts. In the coeliac and other ganglia there are certainly many pre-ganglionic non-myelinated fibers synapsing with similar post-ganglionics. In the peripheral nerves the myelinated fibers must innervate the vessels and glands of the skin, but their stimulation in the splanchnic does not cause constriction of vessels of the mesentery, nor contraction of the gut. What evidence we have points to a difference of function correlated with presence and absence of myelin, but we have not pursued the matter further. The present findings are consistent with the previous inference (Bishop and Heinbecker, 1930) that the *B* wave is that of myelinated autonomic fibers, the *C* wave that of non-myelinated fibers.

In several small strands with 3 to 300 myelinated fibers each, sections were followed through 3 mm. of nerve, and no cases were observed where myelinated fibers lost their myelin sheaths except locally at nodes. While this limited finding is not very conclusive for nerves containing thousands of fibers, it does indicate that loss of myelin is not of general enough occurrence to confuse the histological picture of degenerating nerves stained with osmic acid; nor of normal comparative counts.

Origin of white ramus fibers. It has appeared from previous fiber counts (Lucas and Miksecek, 1936) that a majority of the fibers of the 5th white ramus originated in the dorsal root ganglion. In our preparations after degeneration of both roots, there is so little loss in the white rami that it cannot be certainly detected, although the motor nerves show about half the myelinated fibers degenerating. This is consistent with the estimation from the fiber counts of the numbers of fibers contributed to the rami by motor root and ganglion components, respectively. Further, in favorable preparations where the degenerated motor component ran through or past the ganglion to mix with the dorsal component only well below it, the ramus bundle could be traced definitely into certain well-defined regions of the ganglion containing small cells, separate from the regions where most of the large sensory fibers had their cells of origin. The small white ramus, also, (W_a) not only leaves the trunk before the level at which motor and sensory fibers have significantly intermingled, but it arises from the trunk on the side opposite to the motor bundle, can be traced into the region of small fibers in the ganglion, and does not degenerate after section of the roots. Since physiological experiments indicate that this fine ramus has synapses in the 5th sympathetic ganglion, it seems to contain fibers whose cells of origin are in the dorsal root ganglion but which synapse as motor fibers in outlying ganglia. In cases where the 5th ramus can be traced fairly distinctly through the splanchnic to the coeliac ganglion, large ganglionic masses appear on the fascicle representing it. The

possibility, however, that here one pre-ganglionic fiber might supply many cells of the coeliac ganglion renders the observation less critical than that concerning the smaller ramus to the 5th sympathetic ganglion.

Root stimulation. Stimulation of both 5th roots in the normal preparation has been reported (Bishop, 1937) to induce in the splanchnic only a small *C* wave, and no *B* wave, while stimulation of the trunk below the dorsal root ganglion produced a *C* wave 10 × as high, and a pronounced *B*. We have here observed the results on gut contraction of similar stimulations. Stimulation of the roots causes slight or no contraction of the stomach and gut in our preparations; stimulation below the ganglion causes massive contraction. Contractions of the gut have been reported (Steinach and Wiener, 1895) following dorsal root stimulation in greenfrogs. We find this only if the electrodes are close to the ganglion, and the currents employed only such as to cause heating and drying of the roots at the electrodes. Such currents would presumably spread from the roots into the ganglionic mass.

That this is the explanation of presumed dorsal root activation of the gut seems more probable from the following fact. If roots of either 4th or 5th level are pulled slightly, even after crushing close to the ganglion, good contractions of the stomach and gut follow, almost comparable to those obtained by stimulating trunks below the ganglion. The effect is concluded to be from mechanical stimulation of the ganglion itself, and not of root fibers as such. Since we obtained responses from blood vessels only when the roots are undegenerated, but responses from the gut due to stimulation peripheral to the ganglion in any case, the response of blood vessels serves as a check on the intactness of the roots.

Discussion

No evidence has been obtained about how these fibers from the dorsal root ganglion, capable of activating the gut, receive stimuli in the normal body. The objection to these responses being considered as "antidromic," as various dorsal root responses have been termed, is that the fibers concerned appear not to be afferent, since they do not enter the cord. Further, the work of Tönnies (1938) on "reflex" responses over the dorsal roots raises the question whether "antidromic" is a suitable term to apply to any impulse setting up a peripheral effect. Its use here, as elsewhere, could only serve to cover our ignorance concerning the functioning of these fibers, and would suggest a similarity with the action of fibers which traverse the dorsal roots, which is premature, to say the least. We are, therefore, postponing specific conclusions concerning function until further experiments have been conducted.

Summary

In further investigation of fibers in the sympathetic nerves of the bullfrog, whose cells of origin lie in the dorsal root ganglia, but appear not to send central processes into the roots, the fiber pathways through the sympathetic system have been traced by reconstructions from serial sections and by

physiological recording of action currents. Nerve degeneration procedures were carried out on roots, rami, and trunk.

As a general pattern, with exceptions as noted, the "white" rami from a given level do not have synapses in the sympathetic ganglia of that level, but pass to ganglia at least one level above or below. There are typically two white ramus components, ascending and descending in the trunk from a given level.

The "grey" rami (post-ganglionic) of the 4th and 5th levels consist almost exclusively of myelinated fibers, with myelinated pre-ganglionics.

The splanchnic nerve is made up of rami from the 3rd to 7th levels, the 5th contributing about half the total. Some of the splanchnic fibers arise from cells in the 4th to 7th sympathetic ganglia, some in the coeliac ganglion and some are pre-ganglionic past the coeliac plexus, the positions of the synapses of these fibers being very variable. The coeliac ganglion can be looked upon, therefore, as consisting of parts of the chain ganglia which have migrated further along the fiber pathways. When, as often occurs, there are few cells in the coeliac ganglion proper, ganglia still further peripherally along sympathetic strands presumably represent the same functional elements.

A small white ramus at the 5th level can be traced into the dorsal root ganglion, does not degenerate after section of the roots, and its fibers have synapses in the 5th sympathetic ganglion. The larger white ramus at this level consists predominantly of fibers similarly originating in dorsal root ganglion cells. Most of these fibers course as far as the coeliac ganglion without synapses. Their stimulation after degeneration of the roots causes contraction of the gut, but not of mesenteric blood vessels.

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POSTURAL NECK REFLEXES IN THE LABYRINTHECTOMIZED MONKEY AND THEIR EFFECT ON THE GRASP REFLEX*

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(Received for publication July 6, 1938)

I. INTRODUCTION

THE CHARACTERISTICS of the neck reflexes vary widely among different species, especially between cats and monkeys. It has seemed desirable, therefore, to study them more fully in primate forms, and since the influence of the neck reflexes upon grasping and other prehension phenomena peculiar to primates has not previously been studied, particular attention has been devoted to these reactions. The presence of tonic neck reflexes in the thalamic monkey after bilateral labyrinthectomy was reported by Magnus (1922; see also 1924, p. 441), but his observations were limited to one animal, and the reactions were not studied in detail. For adequate analysis three principal problems must be considered: (i) In what circumstances do tonic neck reflexes appear, *i.e.*, what projection systems is it essential to interrupt; (ii) to what extent does the labyrinth affect the neck reflexes and other reactions of the thalamic state; (iii) the characteristics of the neck reflexes themselves after the labyrinth has been destroyed. The present paper will concern itself primarily with the first and third of these problems; the second can be discussed only briefly.

METHODS

The observations have been made on a group of four rhesus monkeys (*Macaca mulatta*), one green monkey (*Cercopithecus aethiops sabeaus*), and one baboon (*Papio papio*) which had been subjected to bilateral labyrinthectomy for another purpose by one of us (RSD). In each animal the labyrinthectomies were carried out seriatim several months before the cerebral lesions were made. The details of the procedure by which the labyrinth was destroyed are described elsewhere (Dow, 1937).

The lesion essential for bringing out the neck reflexes is a bilateral ablation of the motor projection areas of the frontal lobe (see below). The ablations were made acutely in one labyrinthectomized macaque which was allowed to live 48 hours; in all others the operations were performed with full aseptic precautions. In order to have symmetrical preparations the bilateral ablation in three macaques was carried out simultaneously; in the baboon an interval of 12 days elapsed between the two operations. After the bilateral ablation the animals were completely helpless (Bieber and Fulton, 1938); they were therefore slung in large canvas cradles with a straw burlap bedding, and were tube fed. The longest survival of a labyrinthectomized bilateral area 4-and-6 preparation was 12 days. The completeness of the labyrinthectomy was assured by gross examination after autopsy, and by subsequent microscopical study of the site of labyrinth destruction. The extent of the cortical lesion was also determined by gross examination after fixation of the brain; sample sections were made through the cortical lesions.

* This work was aided by grants from the Research Funds, Yale University School of Medicine and from the National Research Council.

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Principal Observations

Lesions essential for release of the tonic neck reflexes

Neck reflexes can be demonstrated in the thalamic monkey (Magnus, 1922). Such preparations (labyrinth intact) exhibit a characteristic postural pattern which varies in predictable fashion when the animal's position is changed in space; thus when lying in the lateral position the undermost extremities are extended, the uppermost flexed; and the head tends to be elevated toward the horizontal position, especially during the grasp (Fig. 1);

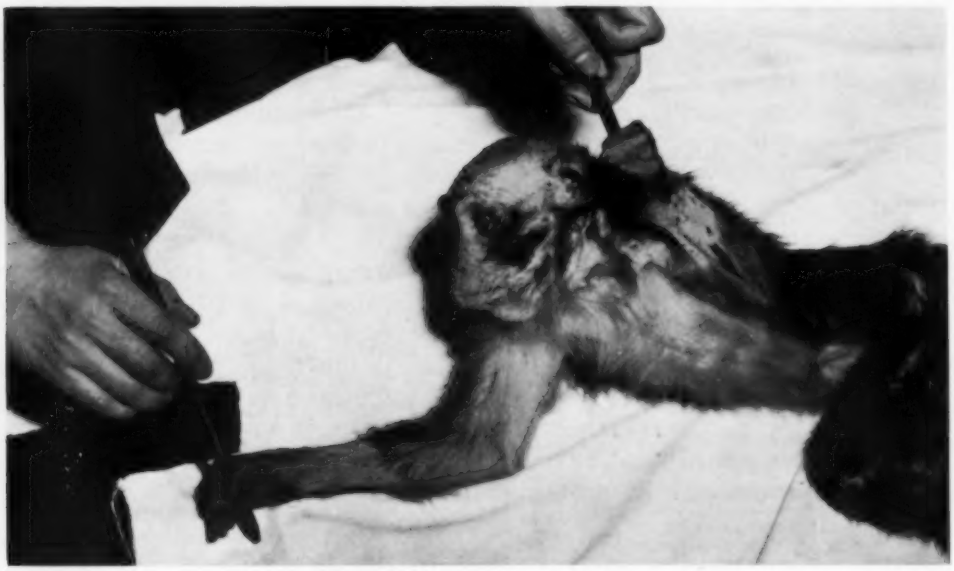

Fig. 1. A macaque in the thalamic reflex status, but with normal labyrinths. Note that the head tends to be held off the table and that grasping is present only in the uppermost extremity.

when turned over the entire pattern reverses. For convenience these stereotyped attitudes have been referred to as "the thalamic reflex pattern." The pattern appears when certain specific cortical projection systems are interrupted. Thus Bieber and Fulton (1933, 1938) observed it in macaques from which areas 6a (upper part) and 4ab of the Vogts had been removed bilaterally (Fig. 2). In such preparations they also found that the grasp reflex formed a part of the postural pattern, being more strongly present in the uppermost limbs and weaker, or absent, in the under limbs when the animal lay on its side (Fig. 1). They inferred from this and other evidence that the grasp reflex is a part of a generalized postural reflex pattern which can be influenced by the labyrinthine, the body righting, and presumably also the neck reflexes. Bieber and Fulton (1933, 1938), however, were able to demonstrate tonic neck reflexes consistently in only one of their bilateral area 4-and-6 preparations; they therefore concluded that some projection systems other

than those arising in areas 6a (upper part) and 4ab must be interrupted before the neck reflexes appear (Fig. 2).

Bieber and Fulton had allowed the face representation (areas 4c and 6a, lower part) to remain intact in their animals. In the present study it has been found essential to remove areas 4c, 6aα (lower part) and 6bα, in addition to areas 6a (upper part) and 4ab, in order consistently to demonstrate the tonic neck reflexes (Fig. 2). We find in animals from which areas 4 and 6 have been

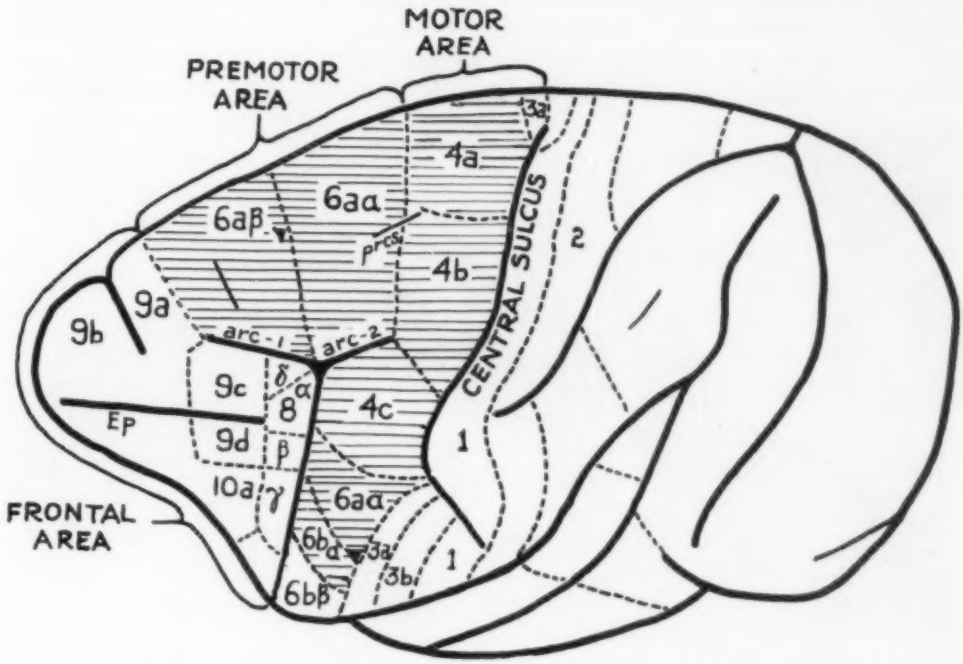

FIG. 2. The Vogt's modification of Brodmann's diagram of the cytoarchitectural area of the cercopitheque cortex. The shaded areas indicate what must be removed from both hemispheres in order to induce the thalamic reflex pattern.

completely removed on both sides, tonic neck reflexes are demonstrable.* Evidently, therefore, the head and neck representation is sufficient to suppress the neck reflexes. Isolated destruction of the face and neck areas, however, in a series of experiments by Green and Walker (1938), did not of itself "uncover" the neck reflexes.

In earlier experiments of Fulton and Kennard (1934) in which areas 4 and 6 were removed seriatim, first from one hemisphere and then from the other, it was observed that a *small portion of one area—be it 6 or 4—of one hemisphere sufficed, if it alone remained intact, to make possible a limited degree of volitional movement in all four extremities.* This small fragment of cortex in one hemisphere also suppressed the thalamic reflex pattern (as we now recognize it), as well as the neck reflexes of both sides of the body. The presence of the tonic neck reflexes in monkeys, and probably also in man, can therefore be taken

* It is probably unnecessary to remove 6bβ, and there is still uncertainty concerning the importance of area 6bα (Fig. 2).

to indicate an extensive *bilateral* interruption of the motor projection systems from the frontal lobes. It is not yet clear whether the projections from area 9 of the prefrontal regions influence the thalamic reflex pattern or the neck reflexes. From the evidence just outlined, one may infer that the influence of these projections is not great in the adult animal.

General effects of labyrinthine destruction

A monkey having areas 4 and 6 completely removed, exhibiting the thalamic pattern, differs in three important respects from such a preparation lacking its two labyrinths. The latter has: (i) absence of head righting reflexes (Fig. 3); (ii) generalized diminution of postural contraction (cf. Figs. 1 and 3); (iii) absence of post-rotatory and caloric nystagmus. Our comparisons are based on animals which were first labyrinthectomized. (We have not yet had

FIG. 3. A labyrinthectomized macaque in the thalamic reflex status following simultaneous bilateral ablation of all of areas 4 and 6, except area 6bβ (see Fig. 2). Note that there is no tendency toward head righting and that the thalamus pattern, though present, is not intense.

opportunity to destroy the labyrinth of an animal from which areas 4 and 6 had been removed as a primary procedure.) The differences between the two animals are conspicuous and may be summarized as follows:

Absence of head righting reflexes. When a bilateral 4-and-6 preparation with normal labyrinths is placed in the lateral position the head may often be held off the table and tend to assume the horizontal position (Fig. 1; see also Fig. 3 of Bieber and Fulton, 1938). When the animal is held upright, the head assumes an upright position as a matter of course; indeed, when the animal is suspended, the tendency toward head righting is clearly apparent. In bilateral 4-and-6 preparations without labyrinths, the head seldom assumes the horizontal position; indeed it wobbles around into any position into which gravity may draw it, and when the animal is placed on its side, the head is not ordinarily raised from the table (Fig. 3).

Generalized diminution of postural resistance. The thalamic reflex pattern is conspicuously present in the bilateral 4-and-6 preparations without labyrinths, and it conforms in all respects with that found in such a monkey with intact labyrinths, except for slight weakness of the grasp reflex and for generalized diminution of postural resistance. Particularly conspicuous is the diminished resistance to passive manipulation of neck muscles, and the corresponding flaccidity of the semi-flexed uppermost limbs when the animal is in the lateral position. *The labyrinth thus appears to give greater intensity to all attitudes of the thalamic reflex pattern* (contrast Figs. 1 and 3), but it is clearly not responsible for the basic pattern itself.

Removal of the labyrinths facilitates the analysis of the thalamic reflex pattern, since turning the animal over or moving through space does not precipitate a "barrage" of labyrinthine righting reactions. In keeping with Magnus' analysis (1922), the sensory origin of the pattern can be traced to asymmetrical stimulation of the trunk and lateral surfaces of the thigh; they thus fall into the category of body righting reflexes acting on the body. With the animal on its side application of uniform pressure to the uppermost surface of the body ("board test") causes the posture of the limbs to become symmetrical, and inhibits the grasp reflex of the uppermost extremities. Pressure on the thigh alone, and especially on the trochanter, equalizes the hind limbs and diminishes the grasp and the asymmetry of the fore limbs.

Rotatory nystagmus. Following bilateral labyrinthectomy in the otherwise intact animal, post-rotatory and caloric nystagmus cannot be demonstrated. If the animal is observed when its eyes are closed or when they are covered by a 20-diopter lens, there is no nystagmus during rotation. If free to fix on objects outside the rotating table, however, a visual or "railroad" nystagmus is seen during rotation. Although this was present in every case prior to the ablation of areas 4 and 6, it was never observed in these animals following ablation of these cortical areas. Post-rotatory nystagmus and caloric nystagmus occur regularly in animals with bilateral ablations of areas 4 and 6, when their labyrinths remain intact.

Neck reflexes and the grasp reflex

The tonic neck reflexes of a macaque with areas 4 and 6 removed bilaterally are similar to those observed in decorticate human beings.* When the jaw is rotated toward the right the right limbs become extended and the left limbs flexed. Exactly the same pattern of response is seen in such preparations when the labyrinths had been previously removed, but all postures assumed are less intense in the labyrinthectomized animals. In these respects the tonic neck reflexes are similar to those described by Magnus (1924) in lower vertebrates. The conspicuous changes in the grasp reflex which occur in association with the neck reflexes have not previously been described.

* It has been pointed out elsewhere (Fulton, 1938) that the majority of reports of human beings exhibiting tonic neck reflexes indicate that the cases in question showed signs, *not of decerebrate, but of decorticate rigidity.*

The grasp reflex changes in intensity with the animal's position in space, being well developed in the flexed uppermost extremities when the animal

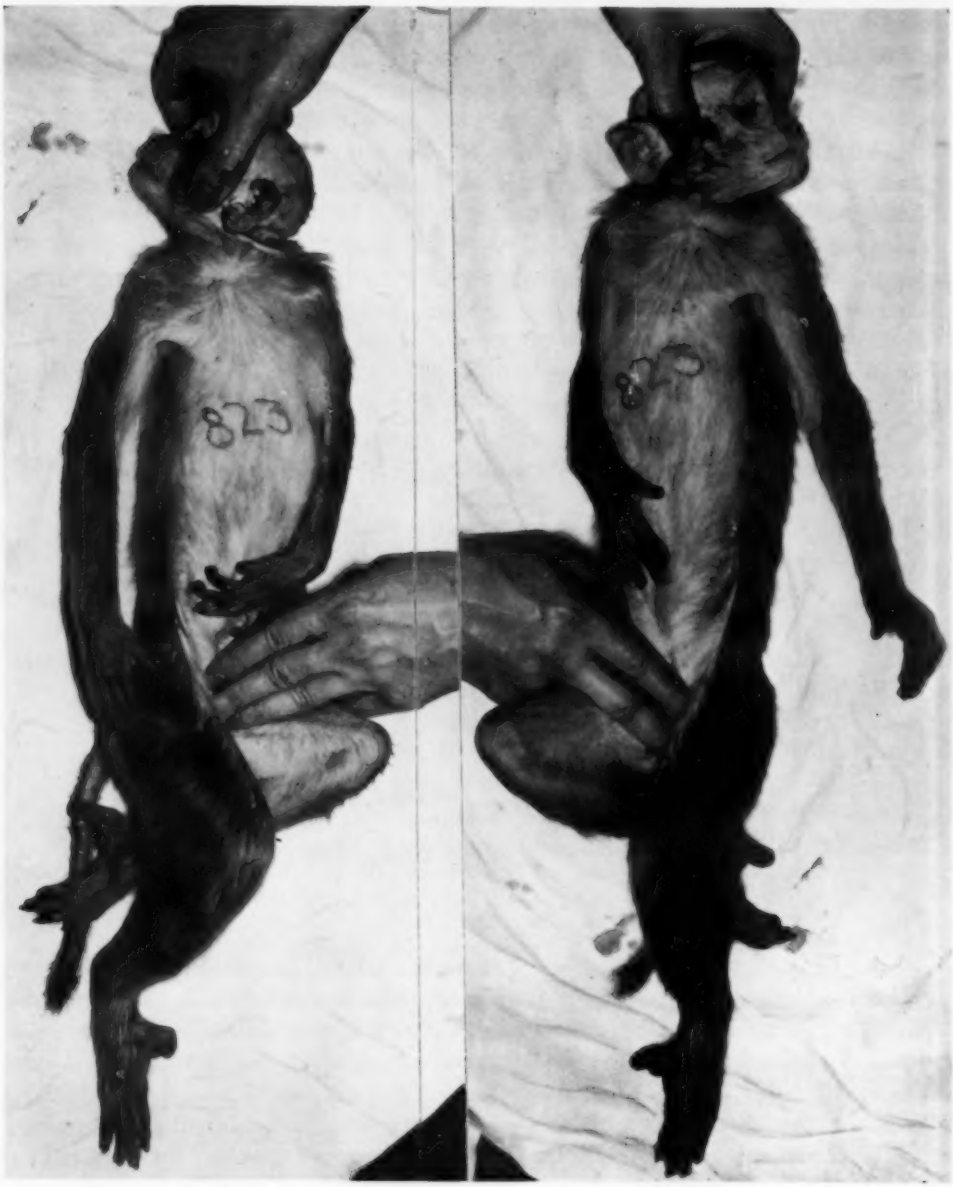

FIG. 4. A. The same animal as in Fig. 3 showing neck reflexes on rotation of the head to the right. B. The same a few seconds later with head rotated to the left.

lies in the lateral position and absent in the undermost extremities (see above). Studies of the neck reflexes indicate that the *grasp reflex is invariably seen in*

those extremities which, through operation of the tonic neck reflexes or of the body righting reflexes, assume a flexed posture. Thus, on *rotation* of the head (a) the "jaw" limbs show: (i) an extended posture; (ii) increase in resistance to passive flexion, and (iii) diminished or absent grasp reflex in both upper and lower extremities; (b) the "skull" limbs show: (i) a flexed posture, (ii) diminished resistance to passive flexion and (iii) conspicuous increase in the grasp reflex of upper and lower extremities. As indicated in Fig. 4A and B these effects are reversed by changing the direction of head rotation. The changes occur after a latency of 1 to 2 secs.

On *extension* of the neck all extremities show: (i) an increase in extensor posture, (ii) increased resistance to passive flexion and (iii) diminution of the grasp. On *flexion* of the neck: (i) all four extremities tend to assume a flexed posture, (ii) resistance to passive flexion is decreased, and (iii) there is marked increase in the grasp reflex, especially of the upper extremities. Other manoeuvres such as rotation of the pelvis produce changes of a similar nature in the hind limbs, *i.e.*, the flexed limb shows the grasp reflex, and the extended limb a diminished or absent grasp.

Discussion

The grasp reflex is released through bilateral removal of areas 4ab and 6a (upper part), but the reaction does not become influenced by the neck muscles until the neck centers are themselves released through bilateral ablation of face areas 6a (lower part) and 4c. In these circumstances the grasp becomes conspicuously influenced by neck rotation, as are the other attitudinal reactions of Magnus. The fact that enhancement of the grasp is invariably associated with an increase in flexor posture is also significant, indicating that grasping is not an isolated reaction, as some have inferred, but rather an integral part of the flexion pattern of postural response in primate forms. As such it is influenced by the neck muscles and no doubt also by the labyrinth. The exact character of the labyrinth's influence on the grasp remains for future analysis, but it clearly takes part in the righting reflex patterns originating in the labyrinth.

Summary

The thalamic reflex status appears in adult monkeys following isolated removal of areas 4 and 6 of Brodmann from both cerebral hemispheres. Tonic neck reflexes can also be demonstrated in such preparations, *provided the motor and premotor face areas (areas 4c, 6a, lower part of the Vogts) have been completely removed from both sides* in addition to areas 4ab and 6a (upper part). The thalamic reflex status has been thus induced in 5 previously labyrinthectomized monkeys and one baboon and the tonic neck reflexes studied in detail. The general reactions are similar to those described by Magnus and de Kleyn for cats and dogs, but the primate shows, in addition, conspicuous changes of intensity of the grasp reflex. When the animal lies supine and the chin is rotated well to the right side, the right extremities become extended and the grasp reflex is absent; the left extremities become flexed and the grasp reflex

is well marked. Furthermore, any postural reaction, whether originating from neck or body, that produces increase of a flexor posture in an extremity also causes *intensification of the grasp reflex;* any postural reaction causing increase in extensor posture causes diminution of the grasp reflex. The grasp reflex in primate forms thus becomes a part of the postural reflex mechanism.

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THE INFLUENCE OF POSTURE ON RESPONSES ELICITABLE FROM THE CORTEX CEREBRI OF CATS

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(Received for publication July 12, 1938)

INTRODUCTION

CLARK AND WARD (1937) described a unipolar electrode by means of which the same point on the cortex cerebri of unanesthetized and unrestrained cats can be stimulated at will over a period of several weeks or more. Using these electrodes they found that like movements could be elicited from a fixed point on the cat's motor cortex from day to day. Occasional variations in these movements were observed, however, when the animal was stimulated after it had altered its posture. These variations occurred after the variables described by Graham Brown and Sherrington (1912), (facilitation, inhibition and strength of stimulating current) were controlled. The present experiments were undertaken to determine the extent of the influence of different postures on movements elicited by stimulation of the motor cortex of unanesthetized cats. The results demonstrate that in an analysis of the mechanisms involved in the production of responses from the motor cortex by electrical excitation the position of the head at the moment of stimulation and also the position of the leg responding to the stimulus are of paramount importance. Emanating from these observations is the idea that stimulation of the motor cortex does not necessarily produce specific movements, but rather that it causes the leg responding to the stimulus to assume a position specific for the cortical point excited.

MATERIALS AND METHODS

Permanent electrodes were placed on the anterior sigmoid gyrus of 22 cats, using the method described by Clark and Ward (1937). The fixed cortical points were stimulated at intervals over a period of several weeks with a weak, 60-cycle sine wave current. The current was taken from the 110 volt lighting circuit and passed through a transformer (Myers, 1936) from which fractional voltages from 0 to 16 could be obtained. For each stimulus a record was kept of the following points: (i) the strength of the stimulating current, (ii) the response in terms of movement, (iii) the latency of the response (the interval of constant stimulation at a fixed voltage before the appearance of the primary movement), (iv) the general posture of the animal, (v) the initial position of the particular extremity in which the primary movement occurred, and (vi) the animal's emotional state at the moment of application of the stimulus.

Kymographic records were made of the responses in some instances. The extremity affected by the cortical stimulus was attached to a heart lever with a thread. The lever was supported by a light spring and directly recorded flexor or extensor movement. One signal magnet marked the time in seconds; another the moment of application and the duration of the stimulus. In order to control proprioception, the extremity responding to the cortical stimulus was deafferented in two animals and in two others the sensory fibers of the first four cervical nerves were cut bilaterally. These animals were studied during the two weeks that they were allowed to survive.

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* National Research Council Fellow, 1936–1937.

The electrodes used were slightly different from those previously described (Clark and Ward, 1937). Cortical injury was reduced to a minimum by having the electrodes pressed firmly against the pia-arachnoid, causing only a slight indentation rather than breaking through. The stigmatic electrode was constructed of a platinum wire fused into a small glass tube with its end rounded in a flame and the wire filed flush with the rounded surface of the glass. The other end of the platinum wire was enlarged with a drop of solder for contact with the stimulating leads. The wire-containing glass tube was then fitted tightly into the threaded end of the stainless steel tube by means of a short segment of rubber tubing. Only the rounded part of the glass (about 1 millimeter) protruded from the threaded end of the steel tube. The remaining construction of the electrode and that of the contact plug with its leads from the stimulating apparatus was similar to that previously used.

Results

Rhythmic and non-rhythmic movements elicited from specific cortical points were studied in the various cats. In general, rhythmic movements may be divided into two parts; the first part is not rhythmic and moves the responding leg (the extremity affected by the cortical stimulus) into a position from which the second part of the movement, the rhythm, occurs. "Batting" and "digging" are examples of such movements elicitable from the motor cortex of cats. In a given animal, with currents of proper strength, the rhythm of these movements develops each time only after the responding leg has been moved by the non-rhythmic portion of the movement (or by hand) into approximately the same position. Ordinarily this position for "batting" is one of partial protraction of the shoulder, partial extension at the elbow and supination of the paw. This position will be called the "final position" for the sake of convenience and for other reasons to be brought out later. In other animals the stimulation of their respective cortical points often evoked simple movements such as flexion or extension with no rhythm. For these movements, also, a "final position" was elicited if the stimulus were of the proper length and strength. The final position for such movements usually appeared to be at the maximal extent of movability of the responding leg in the direction of the movement, *i.e.*, maximal extension or maximal flexion, but this was not always the case. Repeated experiments indicated that under similar conditions of posture and strength of stimulus, the final position for a given cortical point exciting a rhythmic or a non-rhythmic movement was always the same. Stated in another way, the response elicited from a single cortical point was always similar when the same conditions of posture and technic of stimulation obtained for each stimulus.

Variations of the elicited movements induced by altering the position of the responding leg

Figs. 1 and 2 illustrate the variations obtained by stimulating points that produced non-rhythmic and rhythmic movements, respectively, when the position of the responding leg was altered between stimuli. In each instance the stimulus was stopped as soon as the character of the movement was ascertained. In cat 24 (Fig. 1) the response was a movement carrying the right foreleg into a final position of extension with some shoulder protraction.

In this instance the cat was lying on its left side while the left cortex was stimulated at one-minute intervals with a current of fixed strength (2.65 volts). In the first tracing at the number 1, the responding leg was relaxed in a flexed position against the body before the stimulus was applied. The stimulus caused the leg to be partially extended, indicated by the upward direction of the response line. The leg was allowed to remain in the position taken as a result of the stimulus (partially extended) and a repetition of the stimulus (number 2) caused the leg to be further extended. After another minute a third stimulus (number 3) caused the leg again to be extended from the second induced position into maximal extension.

FIG. 1. Cat 24. See text for description of the figure.

By three successive stimuli the leg was moved into the final position. Longer stimulation caused no further movement until a convulsive effect was induced (Ward and Clark, 1938). A single continuous stimulus of about 3 sec. duration in this animal caused the leg to move from full flexion into the final position of maximal extension.

In cat 31 (Fig. 2) rhythmic batting occurred if the stimulus of proper strength was applied long enough. Using only the first part or non-rhythmic portion of the movement it was possible to obtain complete reversals of the response at successive stimuli by placing the responding leg in a flexed position one time and in an extended position the next. A stimulus of constant strength (2 volts) was used in each instance. The cat was lying quietly on its left side and a point on the left motor cortex was stimulated. In the first response the responding leg was passively flexed against the body prior to the stimulus. As a result of the stimulus the leg was moved into a partially extended and protracted position; this is indicated by the downward direction of the curve in the first tracing. One minute later the stimulus was applied again after the cat's leg had been placed in an extended position where the cat allowed it to remain quietly. The stimulus (second tracing) caused the responding leg to be flexed, a complete reversal of the previous effect. The third response was obtained one minute later after the leg had been flexed but

this time less than it had been for the first response. The response was like that obtained with the first stimulus, *i.e.*, downward, indicating extension and protraction, toward the final position. These results could be repeated a number of times without fatiguing the cortical point stimulated if one-minute intervals were maintained between stimuli. Similar results are illustrated in Table I in which a larger number of responses are included.

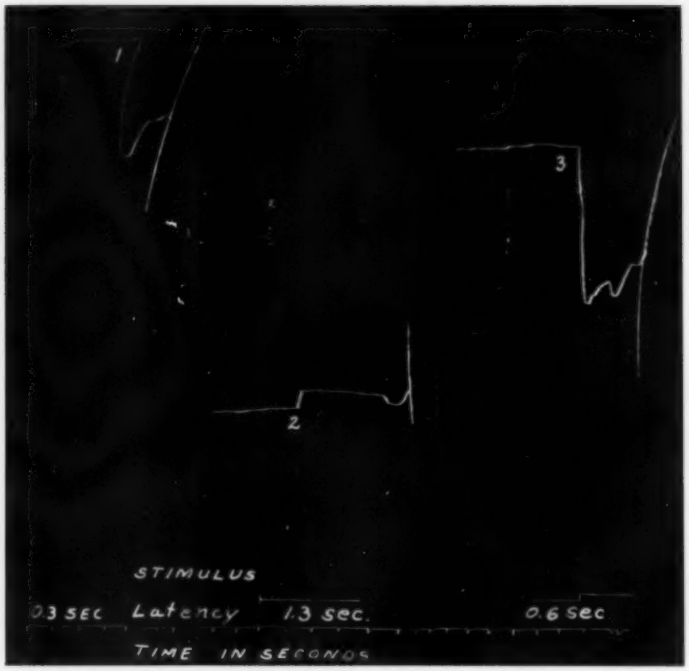

FIG. 2. Cat 31. See text for description of the figure.

From these three examples it is evident that various muscles can be brought into play at different times as a result of stimulation of a single cortical point merely by altering the position of the responding leg prior to the application of the stimulus, and it appears that the stimulation of a cortical point elicits movements that convey the responding leg into a position specific for the point stimulated, *i.e.*, the final position.

Latency variation initiated by altering the position of the responding leg in relation to the final position

The variations in latency (the time between the beginning of the stimulus and the onset of movement) that occur with responses elicited by currents of fixed strength from a single cortical point are great if the stimulus is of the proper intensity. Invariably an alteration of the length of the latency accompanies an alteration in the initial position (the position of the leg when the

stimulus is applied) of the responding leg. This is illustrated in the following examples for both rhythmic and non-rhythmic movements. In cat 24 (Fig. 1) the movement elicited was simple extension and the final position was near or at maximal extension of the responding leg. For the first stimulus when the leg was placed farthest from this position, *i.e.*, flexed against the body, the latency calculated from the coördinates in the figure, was short (0.4 seconds). With the leg in an intermediate position between flexion and extension for the second stimulus, the latency was longer (1.0 seconds), and for the third response with the leg almost fully extended and approximating the final position, the latency of the response was found to be longest (2.4 seconds).

Table 1

Stimulus	Position of Responding Leg When Stimulus Was Applied	Response	Latency
1	Partially flexed	Extension	4.3 sec.
2	Protracted and extended	Slight flexion (withdrawal)	8.4 sec.
3	Protracted and extended	Slight flexion	8.0 sec.
4	Flexed	Extension	4.0 sec.
5	Retracted and flexed	Protraction and Extension	3.9 sec.
6	Flexed, less than in No. 1	Protraction and Extension	6.4 sec.
7	Strong extension	Flexion	4.9 sec.
8	In final position	Rhythmic batting, slow; began with adduction and supination of paw.	10.4 sec.
9	Flexed against body	Extension	2.8 sec.

Cat 36. Rhythmic batting was elicitable in this animal with a long stimulus of 2.5 volts. In most instances, however, the current was applied only long enought to induce a partial response. The cat was lying on its left side and the left motor cortex was stimulated through a permanent electrode. A stop watch was used to measure the interval between the application of the stimulus and the appearance of the movement, *i.e.*, the visible latency of the response.

As pointed out above, the final position for rhythmic batting is often somewhere between full extension and full flexion, and the length of the latency is dependent again on the position of the leg when the stimulus is applied relative to the final position initiated by the stimulus, regardless of whether the starting position of the leg is on one side or the other of the final position. Thus, in the first response of Fig. 2 (cat 31; the movement, rhythmic batting) the leg, when the stimulus was applied, was farther from the final position than in either of the other two responses, and the calculated latency of the extension that occurred was the shortest of the three (0.3 seconds). For the second response the leg was extended slightly beyond the final position and flexion occurred with the stimulus after a long latency (1.3 seconds). For the third response the responding leg was flexed and a distance

from the final position intermediate to the other tests. The latency of the extension that occurred was also intermediate (0.65 seconds). A similar relationship is shown by the latencies of each of the responses listed in Table 1. The starting positions were irregularly altered and the results demonstrate that fatigue is not a factor in the changes in the latencies at successive stimuli delivered at one-minute intervals. It is obvious from these and similar experi-

Table 2

Stimulus Number	Strength of Stimulus (volts)	Latencies		
		Head right	Head center	Head left
1	1.5	8		
2	1.5			4
3	1.5		8	
4	1.1		7	
5	1.1	8		
6	1.1			6
7	1.1			5
8	1.1	6		
9	1.1			4
10	1.1			5
11	1.1	7		
12	1.1			5
Results below obtained the following day; conditions same as above.				
1	1.3			4½
2	1.3	No response*		
3	1.3			4
4	1.3	No response*		
5	1.3			5
6	1.3	No response*		

* Stimulus applied about 10 seconds.

Cat 24. The right motor cortex was stimulated at approximately one-minute intervals, and after each response the responding left foreleg was replaced as nearly as possible in the original position. The response was a simple extension and protraction. The cat's attention was attracted to one side or the other or to the front as indicated in the table. While the head was in a given position, the stimulus was applied and the moment at which movement was noted in the responding leg was recorded. The figures in the three right hand columns are the latencies in seconds of the various responses. In the last series it is noted that with the stimulus used no response was visible when the cat's head was turned away from the responding leg while it appeared consistently when the head was turned toward it.

ments that the length of the latency of a response is related to the distance of the initial position of the responding leg from the elicitable final position decreasing as the leg is placed further (in any direction) from the observed final position.

Effect of variation of position of the head on the final position

That the position of the head of the animal affects the final position elicited is evident from the following experiments. When the head of cat 24 was turned to the right as it lay in a hammock or prone on the table at the

moment of application of the stimulus, the stimulus caused the responding right foreleg to be extended and to abduct. With the head turned to the left the next stimulus caused extension accompanied now by adduction. The extension elicited with the head in the midline was not associated with either abduction or adduction. Care was taken to see that the shoulders did not shift with changes in position of the head. Rhythmic movements, such as batting, could be affected similarly by changing the position of the head. The batting movements were thus directed to either side or to the front by appropriately turning the head to one side or the other or by allowing it to remain forward

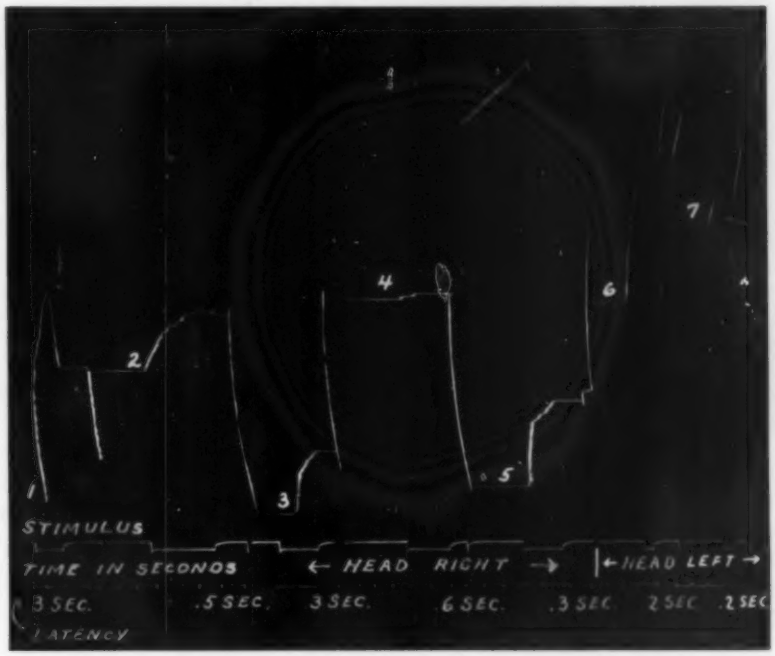

FIG. 3. Cat 25. See text for description of the figure.

when the stimulus was applied. Further, raising the head during the stimulus led the responding foreleg to flex more at the elbow so that the batting took place on a higher plane than before. Lowering the head similarly caused batting in a position more nearly under the animal. These observations make it appear that the leg final position elicited from a fixed cortical point shifts with the head position so that it follows the nose of the animal. Similar results were obtained with the animals blindfolded.

Effect of the position of the head upon the latencies of the responses

During experiments conducted on cat 24 while it was lying sphinx-like, there were variations in the latency of the responses of the foreleg which

appeared to be related to the position of the cat's head during stimulation. Examples of such results are recorded in Table 2. They indicate that the latency is shortest when the head of the animal is turned (lateral flexion) toward the responding leg and lengthened when the head is turned away from it. Kymographic records of the responses elicited from cat 25 (Fig. 3) show a similar relationship. A point on the right cortex was stimulated with currents of fixed strength (4.25 volts) at one-minute intervals. The response, extension in the left foreleg, is indicated by an upward movement in the figure. The first five responses were obtained with the head turned towards the right and show longer, calculated latencies than do the later ones. This occurred even though in the later tests the initial leg position was closer to the final one, so favoring a longer latency.

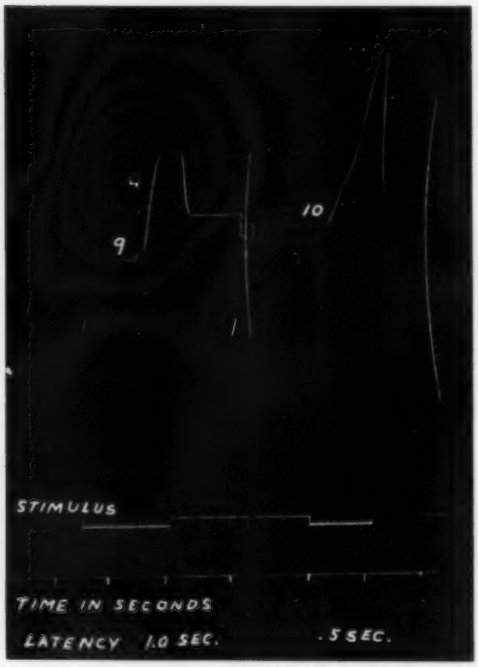

FIG. 4. Cat 25. The animal was lying prone in a body cast with its legs freely movable. It had received 10 milligrams of nembutal two and one half hours prior to the experiment (in other experiments it has been observed that approximately 15 milligrams per kilogram of body weight will cause a loss of the placing reactions in the cat for only thirty to forty minutes). The right motor cortex was stimulated with currents of fixed strength (1.75 volts) at one-minute intervals. For the first response (marked with a number 9) the cat's head was down and in the midline. The response was simple extension of the leg occurring after a calculated latency of 1 second. The cat's head was then raised so that the nose-occiput angle was 45° above the horizontal and held there for the second stimulus. This response (marked with the number 10) contained in it some protraction with the extension, and the calculated latency was 0.5 seconds.

A number of responses, about 10 each in one experiment, were obtained with the animal's head turned to either side and the latencies averaged for each position. These records also showed that the latency when the head is turned away from the responding leg is about 10 per cent longer than when turned toward it. Such observations were not obtainable in all animals studied.

The length of the latency was also altered characteristically by holding the head in a raised or lowered position. As is shown in Fig. 4, the latency is shorter when the neck is extended and longer when it is flexed forward. The animals were quiet in these and other similar experiments.

Effect of deafferentation of the responding leg on latency of responses

In two animals the lower five cervical and the first two thoracic dorsal roots on the right were sectioned extradurally. The general pattern of the responses elicited in the deafferented leg of each animal during several weeks after its operation was similar to that obtained before, but the movements were jerky and poorly coördinated. Rhythmic batting was elicited in one of the animals. Other than the jerkiness of the movements, the only effect of the dorsal root section was to make remarkably constant the latency of the response for a given strength of stimulus regardless of the initial position of the responding leg. Increasing the strength of stimulus shortened the latency.

Effect of bilateral section of the first four dorsal roots on the final position and on latency

Because the final position elicited from a given cortical point appeared to shift so as to follow the nose with changes in the position of the head, the first four cervical sensory roots were sectioned on both sides (motor and sensory components of the first and the second nerves were cut outside of the vertebral canal at their exit from the latter, and the dorsal roots of the third and fourth cervical nerves were sectioned extradurally). In two animals tested during two weeks after operation, turning the head to either side or flexing or extending it did not produce the normal shift in the elicited final position, and latencies with currents of fixed strength were independent of head position. These findings were repeated frequently in the two operated animals during the two weeks of their survival.

Effect of environment on the latency of the responses

Bubnoff and Heidenhain (1881) have shown in dogs anesthetized with morphine that the latency of a response elicited electrically from the motor cortex is shortened by a few hundredths of a second as a result of coincident cutaneous nerve stimulation. Variations of remarkably greater magnitude were observed in the present experiments on unanesthetized cats as a result of normal cutaneous impulses or by auditory stimuli given just prior to the cortical ones. Figure 5 illustrates this in cat 37, a normal animal. The cat was lying on its left side, and the left cortex stimulated at one-minute intervals with a current of fixed strength (2.5 volts). The response in the right foreleg was retraction at the shoulder and flexion at the elbow. The letters under the responses indicate the following: *R*, the animal was undisturbed for about 1 minute; *P*, the cat was rubbed briskly 10 seconds before the application of the stimulus; and *S*, a sharp sound was made a few seconds before the application of the stimulus. Similar results to those shown in the figure could be obtained repeatedly with stimulation of the cortex. It is evident from the variations in latency demonstrated in the figure, that unusual noise or handling of the animal may reduce their length by almost one half. The state induced by these procedures lasts for a variable interval from a few

seconds to minutes depending on the disposition of the animal. In the cited experiments, the original latencies were obtained after a one-minute respite. Such vacillation of the latency under the influence of various environmental conditions may be of considerable importance in determining a threshold for cortical points in the unanesthetized or lightly anesthetized animal.

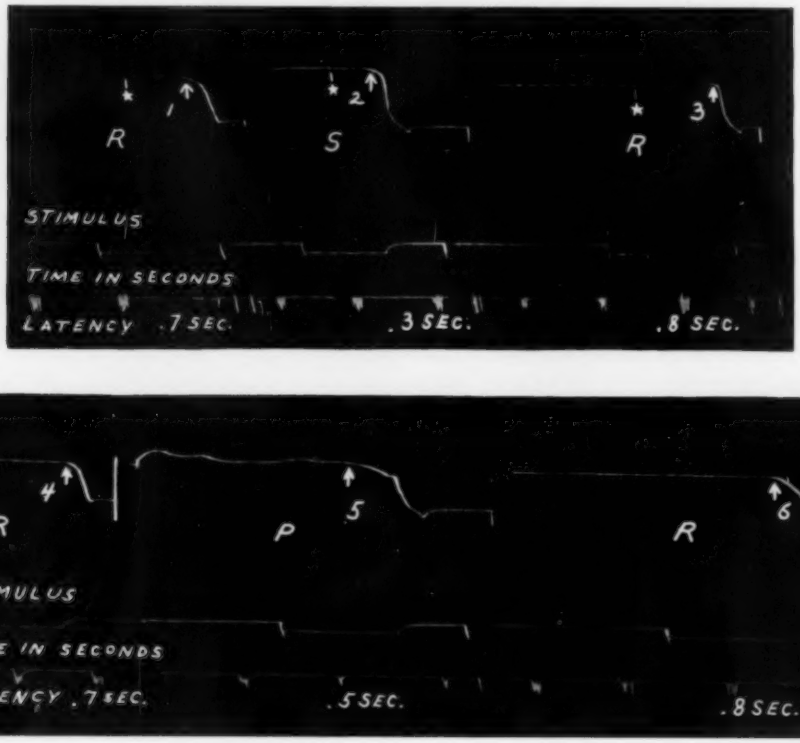

FIG. 5. Cat 37. See text for description of the figure. In the first three responses the stars indicate the moment of application of the stimulus, and the arrows indicate the beginning of the response.

DISCUSSION

The question of the stability of a motor cortical point in relation to the movement elicited from it by electrical stimulation has been of great interest not only in the study of cortical physiology but also in the study of pathological states which involve the cortex and deal with cortical localization of function. It has been shown (Clark and Ward, 1937, p. 16) "that the same response can be elicited from the same cortical point from day to day, and (the experiments) argue against any marked instability of cortical points except under the temporal influence of transient physiological states." This generalization is borne out by the present experiments, which demonstrate some of the fundamental factors responsible for alterations in the movements elicited by electrical stimulation of fixed cortical points in unanesthetized animals.

It appears that neither specific muscles nor specific movements are necessarily represented under specific points on the motor cortex, although the same movements can be elicited repeatedly at will by stimulation of a cortical point if the posture of the animal is unaltered. Rather, electrical excitation of a cortical point causes the responding leg to assume a more or less constant position. This position has been called the final position, and the movements that occur in attaining it may be many and varied, depending on the position of the responding leg prior to the application of the stimulus. Further evidence that such a point specificity exists in the cortex is found in the observations that the length of the latency of the responses varies inversely to the distance of the initial position from the final one.

The explanation for the constancy of latency (with fixed stimuli) after deafferentation of the responding leg is not clear. It is evident, however, that the variation in latency associated with initial position of the responding leg is dependent upon the proprioceptive afferents of that leg. This suggests that tone is an important factor in controlling latency; especially since Sherrington (1921) has shown that tone is fundamentally associated with a proprioceptive reflex. As further evidence, the animal's general state of excitement (general bodily tone) often determines the length of latency, and also increased activity of tonic neck reflexes tends to shorten the latency, other factors being constant.

The effect of the tonic neck reflexes was first demonstrated on a background of extensor hypertonus in the decerebrate animal by Magnus and de Kleijn (1912) and later (1915) in certain pathological conditions in man. Lissitza and Pentzik (1934) have studied the effect of the tonic neck reflexes on the contralateral legs of conscious dogs for a few days after removal of cortical area 4 on one side. Hines (1937) has observed the influence of these reflexes on the posture of the legs in a monkey as long as 20 months after the bilateral removal of areas 4 and 6, exclusive of the face areas. In the present experiments changes in the position of the head have been shown to cause a shift in the final position, which seems to follow the nose of the animal. Most of the change occurs at the shoulder girdle. This dependence of final position on head position is lost if the sensory fibers of the first four cervical nerves are cut bilaterally, thus again demonstrating the importance of the neck reflexes. Somewhat similar changes in the position of the leg in rhythmic activity are caused by slight shifts in the position of the stimulating electrode in acute experiments on anesthetized cats (Ward and Clark, 1935). An altered electrode position, however, cannot explain these results in the conscious animal since the shift in final position is lost after deafferentation of the upper cervical region. This relationship between the head position (acting through the sensory fibers of the upper cervical nerves) and the final position of the leg demonstrates how postural reflex activity may coöperate with cortically initiated activity to insure coördinated responses with the least effort on the part of the higher centers.

The differences in latencies of individual responses, which result from

altered head position, were often variable and small. Nevertheless, the interpretation that they are the result of tonic neck reflexes acting on the responding leg is strengthened by the fact that deafferentation of the neck muscles (supplied by the first four cervical nerves) obliterates them. The variability in the results might be explained on the basis of an altered state of excitability of the animal at the moment of stimulation; because, as has been shown, the level of excitement has a marked influence on latencies for successive stimuli at a given cortical point. Sherrington (1920, p. 232) has said that, "The tonic reflexes of attitude are of habitually low intensity, easily interfered with and temporarily suppressed by intercurrent reflexes, these latter having higher intensity." Even though the "reflexes of attitude" persisted in such a field, their intensity is so low that their comparative influence from stimulus to stimulus could easily be masked by the more potent effect of this rapidly changing general excitatory (emotional) state of the animal.

The question of a possible effect of the labyrinths on the latency of responses and on changes in the final position with altered head positions naturally arises. No experiments were done directly to test their effect. The observations on the influence of head position were made when the head was stationary; and, except when the head was in a raised or a lowered position, the nose-occiput angle with the horizontal was approximately the same in each instance. Figure 4 may find part of its explanation in the effect of the labyrinthine mechanism because Magnus (1924) has shown that a greater increase in tone is occasioned in the forelegs by this mechanism when the head is back ("plus 135°") than when it is bent forward ("minus 135°"). Since changes in the position of the head produced no effect on the final position or on the latencies after deafferentation of the upper cervical region, it seems likely that the labyrinthine mechanisms do not play an important part in these processes, at least under such conditions.

Numerous methods have been employed to determine how skeletal muscles coöperate to produce smooth and effective motion. These have been presented in complete form by Tilney and Pike (1925) who discuss the relative merits and demerits of the various procedures. Using the method employed by the Sherrington School, in which the leg was fixed and strings were fastened to the detached tendons of antagonistic muscles so that their movements were recorded simultaneously, they observed irregular variations in the simultaneous activity of the antagonistic muscles of the leg, induced by electrical stimulation of the motor cortex. It appears likely that this variability was due to altered proprioceptive impulses coming from the antagonistic muscles whose tendons had been cut; for with a given initial posture of the responding leg (normally innervated) and a known final position elicitable from a particular cortical point, we can predict for each stimulation the resultant contractions of groups of muscles in terms of movement and even the relative latency of the responses.

Summary and Conclusions

1. Under fixed conditions of posture, localization of function in the motor cortex appears to be constant in that a specific "final position" is elicited in the leg affected by the stimulus.

2. By altering the position of the responding extremity over a wide range, before each stimulus to a fixed cortical point, the movement elicited may be altered and even reversed, but the same final position will be attained each time (other postural factors constant).

3. Differences in latency of responses for different initial positions of the responding part support the conception of a final position.

4. The final position is modified by certain postural reflexes.

5. The latency of responses is markedly influenced by the general emotional state of the animal at the moment of stimulation; thus a variability of the "threshold" of cortical points can occur even with currents of fixed strength and for fixed postures.

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TABLE OF CONTENTS

Vol. I, No. 5

JOURNAL OF NEUROPHYSIOLOGY